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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

GALLOWAY, J. F. **Integration of Preventive and Curative Health Services through Comprehensive Local Administrative Units.** *Lancet.* 1960, July 2, 34–6.

The author is the medical officer of health of Wolverhampton.

The first point made in the paper is that the National Health Service Act, 1946, reversed a century-old trend towards the local administration of all health services. This was done by "sacrificing the local authorities' hospital services to ad-hoc regional boards". Now after 12 years the good and bad points of this reversal are recognizable.

The author expresses the opinion that this reversal of the previous trend was for 2 main reasons: (1) some local administrative units are too small to meet present-day needs and (2) most doctors consistently refuse to work under local government. He relies on the Local Government Commission now at work to produce "efficient and effective administrative units". He thinks that as a result doctors will be "less suspicious of the vagaries of democracy".

He believes that when local government is reformed the 3 branches of the National Health Service can be brought closely together and the service administered as a whole. For this it will be necessary for the units of administration to be geographically co-extensive.

He sets out cogently the advantages which would ensue. Only when the same authority holds the purse strings for both hospital and community care can money be spent efficiently and when the administration is local, people with grievances can readily approach those responsible. Hospital management committees should be statutory committees of a local authority, as Education committees are, but one-third of their membership should be medical. He recalls the recommendation in 1926 of the Royal Commission on National Health Insurance to the effect that the local committees for the medical services should be under the control of the local authority.

Regional Hospital Boards should continue but with curtailed executive responsibilities. He gives details of who should pay the various officers and concludes: "There are powerful arguments in favour of comprehensive health services based on local administrative units, the formation of which is within the power of the existing Local Government Commission. Parliament is becoming dissatisfied with the control of the National Health Service; local authorities are dissatisfied with the existence in their areas of independent organisations serving the local population and maintained out of public funds; and the public are dissatisfied with their inability to inquire, question, or criticise". [This well-written and timely paper follows the line of the Reservation to the Guillebaud Report of 1956 written by Sir John MAUDE (see this *Bulletin,* 1956, v. 31, 1053). The prerequisite for action is the reform of local government, a subject which bristles with difficulty. *Allen Daley*

CENTRO SPERIMENTALE PER L'EDUCAZIONE SANITARIA [MODOLO, M. A., Director.]. L'educazione sanitaria nella scuola e nei programmi scolastici. [**Health Education in Schools and School Syllabuses**] 121 pp., illustrated. [24 refs.] 1960. Perugia.

The symposium which was held at this Perugia centre had been promoted by the Italian Federation against Tuberculosis and sponsored by the Ministry of Education.

A. SEPPILLI, Director of the Perugia Institute of Hygiene, dealt with *Health education* (pp. 33–39). In Italy, the expectation of life was 33 years for men and 34 for women when public health measures were introduced in 1888: by 1950–53 these figures had improved to 71 and 74 years. Scientific progress and international health agreements and organizations have now conquered many infectious and other diseases, but there are other diseases which show high morbidity and high mortality and cause social and economic losses. Degenerative conditions of the cardiovascular system, malignant growths, and diseases of the nervous system and of the mind are instances, and it is more than ever important to educate

the public with regard to their prevention and control. Seppilli draws a distinction between hygiene propaganda by subliminal techniques, and health education which aims at achieving conscious and lasting changes in behaviour for the sake of better health: the techniques will vary with the age, social and other group characters of the persons who are being dealt with. Many audio-visual aids are now available, discussion groups are valuable and good planning and organization are essential.

G. CALÒ, who is President of the National Didactic Centre, discussed *School and Health* (pp. 41–49). Psychosomatic knowledge in general medicine and in the treatment of mental disease and deficiencies provides lessons on which to base health education, and much can be learnt from successful public health measures already put into practice. School activities should be planned so as to satisfy the requirements of health and hygiene. The interaction between pupil and teacher, and even the behaviour of the latter, may call for appropriate action from time to time. In the light of their effect on mental and physical health, periods of teaching and of rest, size and form of syllabus must be carefully balanced and an amount of home-work given which will not prejudice adequate sleep; there must be sufficient provision for athletics, games and physical exercise. Premises and school environment must come up to the standards of hygiene which are being taught. School medical officers should be appointed and given authority to exercise necessary control.

C. COTTONE, who is an Inspector from the Ministry of Education, took *Health education and the school syllabus* (pp. 51–61) as his subject. We criticize, from the angle of health, the mounting weight of the school syllabus, and we are liable to contradict ourselves if we recommend the teaching of hygiene as a separate subject; such teaching can be integrated into the background of other subjects, both theoretical and practical. Infant, elementary and secondary schools have differing scopes: the first are a continuation of home training, mainly in behaviour, and the infant pupil is taught to be a fitting member of his community of fellow-infants. The main aim of the elementary school is the development of a taste for knowledge; it is wasteful to burden the child with an excess of learning which is dependent on memory and is completely lost as the child grows. Elementary schools in Italy do not at present adequately allow for physical training. The teaching of biology offers a usefu medium for health education in schools. The physica and mental health of the teachers is relevant: in 194 [why choose this war year to quote?] tuberculosis morta lity among teachers was 1·52 per 1,000.

C. VETERE, a Provincial Medical Officer of the Ministr of Health, spoke of *Health education and the training c teachers* (pp. 64–75). Hygiene does not appear as specific subject in the syllabus of Teachers' Trainin Colleges, Higher Secondary Schools and Universit Institutes, and yet if planned along practical lines suc training need not be a burdensome addition to the pro gramme. The training and experience of school medica officers make them eminently suitable to lecture on, an demonstrate, hygiene to teacher trainees. The study c infant and youth psychology is important. Adolescen are keen to know about the physical and mental workin of their own bodies, and their teacher must be competen to answer their questions satisfactorily and factuall Vetere suggests ways by which hygiene can be made to fi integrally into the rest of the syllabus.

L. MESCHIERI writes on the *Contribution of the schoo towards mental health* (pp.77–99).

M. A. MODOLO, Director of the Experimental Centre Perugia, dealt with the *Aspects of child psychology a health education* (pp. 101–107): the latter is made up c the day-to-day life of teachers and pupils in its variou personal and environmental aspects, rather than bein just a lesson to be taught and learned.

Study groups discussed a number of subjects and short account is given of each. There is also a no on the recommendations and conclusions which wer adopted at the end of the symposium. *J. Cauchi*

GHOSH, Birendra Nath. **A Treatise on Hygiene an Public Health with special reference to th Tropics.**

This book was reviewed on p. 1067.

HANLON, J. J. **Principles of Public Health Admini tration.**

This book was reviewed on p. 1069.

VITAL STATISTICS

RING, Eileen M. **A Study of Perinatal Mortality in England and Wales.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, June, v. 19, 84–97. [27 refs.]

The trend of perinatal mortality (stillbirths plus deaths under one week) has been reviewed for the 30 years 1928–58. The rate rose from 60·8 per 1,000 total births in 1928 to 63·4 in 1933 and then fell fairly steadily to 37·7 in 1950 and in the last 8 years has fluctuated arou a fairly constant level although the rate in 1958, 35 was the lowest ever recorded. The rate in England an Wales is much higher than in some other countries. The was considerable regional variation, from 44·43 in sou east Wales to 31·41 in London and the south east regi in 1956. The author has made an extensive review of t findings of other workers and compared their co clusions. Important factors affecting the rate are matern age, parity, multiple pregnancy and social class. T

causes of perinatal mortality are difficult to classify, obstetricians tend to classify by the condition of the mother and pathologists by a pathological condition, and generally the pathologists will not accept prematurity. Whichever way the deaths are classified a large proportion fall into a group of unknown causes. It appears that up to two-thirds of the deaths are among premature infants and for over half of these no medical cause can be given. The chief maternal factor is toxaemia of pregnancy and the most important causes of perinatal mortality are prematurity, asphyxia and atelectasis, birth injuries and congenital malformations. *W. J. Martin*

EPIDEMIOLOGY

GENERAL REGISTER OFFICE. **Studies on Medical and Population Subjects No. 14. Morbidity Statistics from General Practice. Vol. I.** (General) [LOGAN, W. P. D. & CUSHION, A. A.]. pp. iv + 174, 1 fig. & 4 diagrams. 1958. London: H.M. Stationery Office. [15s. 6d.]

This volume contains a description of a statistical study of the clinical records of 106 general practices in England and Wales during the 12 months May 1955 to April 1956 carried out jointly by the College of General Practitioners and the General Register Office.

The object of this survey was, in essence, the measuring of the amount of sickness encountered in general practice, since morbidity statistics are at present scanty and incomplete. The survey was limited to National Health Service patients on the lists of doctors in these 106 practices widely distributed geographically throughout the country. Of these practices 45 were in the north of England, 18 in the Midlands and Wales and 43 in the South; 63 were classified as urban, 20 as semi-urban and 23 as rural.

Separate chapters cover (1) general considerations and organization, (2) methods of record-keeping, record cards and processing of records, (3) the presentation of results, (4) determination of populations, (5) commentary on the statistical tables which are presented, and (6) conclusion.

The tables of data occupy about 120 pages. The statistics give "for a large and representative sample of the population of this country, a conspectus of the sickness that led them to consult their doctor over the course of a continuous 12 month period, and indicate, with an accuracy sufficient for most purposes, not only the volume of medically treated sickness encountered but its distribution by diagnosis, sex, age, and (in the next volume) occupation". This general practitioner morbidity survey represents "an important pioneer advance in the technique of morbidity measurement" and also provides "for the first time on a major scale, a comprehensive collection of morbidity statistics for the general population of this country".

"It is intended in a second volume to consider occupational aspects of morbidity, while a third volume will discuss the findings of the survey from a more clinical viewpoint". *M. E. Delafield*

MATERNAL AND CHILD HEALTH

NASH, F. W. **A Review of all Births in Merthyr Tydfil, 1955.** *Med. Officer.* 1960, July 15 & 22, v. 104, Nos. 3 & 4, 55–61; 75–80. [33 refs.]

The author is a consultant paediatrician.

The paper is a detailed study of 881 maternities and 887 births which occurred in 1955 with a perinatal mortality rate of 47·4 per 1,000 total births which exceeds the rate for England and Wales by 26·7%.

Merthyr Tydfil is a Welsh county borough of 59,900 inhabitants. It is an industrial town, mostly engaged in steel production and coal mining, which has had more than its share of unemployment.

The perinatal mortality which reached 72·3 in 1953 has always been high. The 1955 figure of 48·4 includes a stillbirth rate of 33·0.

The obstetrical services for the district are described. The special nurseries for immature babies and the unit for haemolytic diseases are in Cardiff 24 miles away.

The social structure of the population, compared with Wales as a whole, shows a substantially lower proportion of the higher income groups, Classes I and II and a higher proportion of the intermediate groups, Classes III and IV but for Class V it is similar to the rest of Wales. The heaviest rates for stillbirths, 39·5 per 1,000 and perinatal mortality 55·7, were in Social Class III: these compare with rates of 31·6 and 47·4 for all the infants in the survey. The rates are relatively unchanged when adjusted for maternal age and parity. The illegitimate birth rate in Merthyr is low.

Institutional confinements were 70% of the total but only 26% of them were in a hospital providing specialist care for all cases. The perinatal mortality for institutional births was 46·1 and for domiciliary 49·1. Ante-natal care was good for 51·3% of the mothers: none or sparse for 7%: intermediate for 37·5% and not known for 4·2%. The perinatal mortalities were 42 for Grade I, 32·8 for the intermediates and 112·9 for those who had little or none.

Of the 881 pregnancies 179 were in some way complicated or abnormal: 151 of these mothers were delivered in institutions and 28 at home. Analysis of

the abnormalities showed that 78 were due to toxaemia in some form and 26 to antepartum haemorrhage. The perinatal mortality among the offspring of the toxaemic mothers was 137·5 and among those mothers with non-toxaemic abnormalities 134 but where the pregnancy was normal it was only 22·9.

In 39 mothers labour was induced and in this group the perinatal mortality was 116·7.

The perinatal mortality when the presentation was a normal vertex was 32 but among the 37 births where it was a breech or face it was 351.

The rates of immaturity were 10·3% of all births; 9·4% of live births and 35·7% of stillbirths. The perinatal mortality among the immature was 230·8 and for the full-term 26·4. A study was made of the factors causing immaturity but no new facts were established.

The discussion points out that, as the numbers involved are small, firm conclusions cannot be drawn from the results. It will be helpful when they can be compare with similar studies in other areas and with the pendin report of the National Birthday Trust. The suggestio that the persistent high mortality is an expression o " generation mortality " and a result of the austerities o a generation ago cannot be proved. What is remark able is the high mortality in Social Class III. It probable that ante-natal care could be improved. It difficult in this area to accept the " often quoted opinio that pregnancy and labour are normal, physiologica processes ". They are certainly not for the infants.

Allen Daley

MILLER, F. J. W. *et al.* **Growing up in Newcastle upo Tyne. A Continuing Study of Health and Illnes in Young Children within their Families.**

This book was reviewed on p. 946.

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

BERG, G. & TILLMAN S. **The Care of the Chronically Ill in a District in Sweden. A Medical and Social Investigation.** *Canadian Med. Ass. J.* 1960, June 11, v. 82, No. 24, 1229–35.

This paper gives detailed information about the care of the chronic sick and the aged in the county area outside Stockholm.

Analysis of the ages of patients admitted to the medical wards of acute hospitals during the last 20 years shows a decline from 21% to 11% of the total admissions for the age-group 15–30 years, an increase from 12% to 20% at ages 65–75 and from 3% to 13% at ages over 75. The change in surgical wards is similar. The types of illness have also changed, and chronic diseases of the cardiovascular system, kidneys and joints are replacing tuberculosis, acute rheumatic conditions, pneumonia and the acute infections.

A study has been made of all the chronic patients in the county for whose care a public contribution has been asked. They numbered in all 658: 143 were in the county nursing home for chronic cases; 33 in private nursing homes; and 247 in homes for the aged; the rest were at home. There were 230 men and 428 women. For every 1,000 persons over 67, which is the normal age for receiving old-age pensions, 42 suffer from a chronic ailment. A table shows the diagnoses with age and sex distribution. A single medical officer examined all of them and divided them into " pure chronics " *e.g.* those in need of both medical and nursing care and " othe chronics " needing medical but not nursing care. Th table divides them similarly. Of the 393 pure chronic 27·7% had had a cerebral haemorrhage, 17·3% ha chronic rheumatism of the joints and 10·9% organi nervous diseases. The percentages for these condition among the 265 other chronics were 10·6, 8·3 and 5·7.

Those with mental disease formed the largest grou among the " other chronics ", 24·5%. Chronic diseas is not confined to the elderly; there were 2·9 per 10,0 population at ages 10–50; 33·5 at 50–65, 186·6 at 65–8 and 868·7 at 80+. For pure chronics the figures a 2·0, 20·0, 117·0 and 468·1. 423 of all chronics (658) we in hospital and 266 of the 393 pure chronics.

An attempt is made to calculate the probable numb of beds which will be needed at the end of 1970. Th calculations are based on 4 groups, (a) all chronics, (pure chronics, (c) all chronics who need institutional ca (d) pure chronics needing institutional care. For total population of 591,000 the results are (a) 2,069, (1,233, (c) 1,322 and (d) 831.

Preventive measures are not very helpful, but ear diagnosis and treatment, especially by the physiotherap will often avoid the need for admission to hospital. Th chronic group is by no means homogenous and in asses ing the need for beds, regard must be paid to the varyi incidence of the different diseases. The absence of usef work and enforced idleness appear to bring on illness.

Allen Daley

CANCER

BRITISH EMPIRE CANCER CAMPAIGN. **Thirty-Seventh Annual Report covering the Year 1959. Part II. The Scientific Report of the Researches undertaken by the Central Organisation and its Autonomous Councils in the United Kingdom, and by some of its Affiliated Organisations Overseas.** pp. xli–liv + 666. [Numerous refs.] 1960. London: 11, Grosvenor Crescent, Hyde Park Corner, S.W. 1.

This massive Report covering the year 1959 on research work carried out with support from the British Empire Cancer Campaign, embodies contributions from about 35 University centres and other institutions, and from about 50 individual workers in the Empire. These contributions with their lists of publications and references contain so great a wealth of new knowledge on the many aspects of the cancer problem that it would probably be impossible to produce an adequate index. The introduction to the Report alludes to only a proportion of these researches in the fields of carcinogenesis, chemotherapy, tumour immunology, virology, clinical and surgical pathology, and radiotherapy and radiobiology.

An impressive body of work has been done on the chemistry and physics of carcinogenesis. It is hopeful to read that there is now a "slow but continuing increase in the efficiency of chemotherapeutic agents of classes already known, and the extent to which both these aspects are being influenced by the revival in tumour immunology".

The difficulties of inter-relating the results of researches in different aspects of the problem are obvious, but as is stated in the summary to the report "it will be a main task of the next few years to reach a synthesis in our knowledge of chemical and viral causation — aspects at first sight inconsistent or exclusive, but by no means necessarily so. It is a legitimate hope that this kind of synthesis will lead in turn to methods of control, based upon true understanding of the essential differences between normal and cancer cells". *M. E. Delafield*

MUIR, C. S. **Cancer of the Lung, Trachea and Larynx in Singapore.** *Brit. J. Cancer.* 1960, Mar., v. 14, No. 1, 1–7, 1 fig. [23 refs.]

The morbid anatomical features of 176 lung, 2 tracheal and 13 laryngeal cancers are described. They do not differ from those seen elsewhere. Available statistics indicate that cancer of the lung at present accounts for about 10–15% of all malignant tumours in Singapore, and a review of the literature shows that it is to be found throughout Asia. *A. Bradford Hill*

D'CONOR, G. T. & DAVIES, J. N. P. **Malignant Tumors in African Children, with special reference to Malignant Lymphoma.** *J. Pediatrics.* St. Louis. 1960, Apr., v. 56, No. 4, 526–35, 3 figs. [19 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 1219.]

BORNEFF, J. & KNERR, R. Cancerogene Substanzen in Wasser und Boden. III. Quantitative Ermittlungen zur Löslichkeit, Filtration, Adsorption und Eindringtiefe. [**Carcinogenic Substances in Water and Soil. III. Quantitative Investigations on Solubility, Filtration, Adsorption and Penetration**] *Arch. f. Hyg. u. Bakt.* 1960, March, v. 144, No. 2, 81–94. [11 refs.]

BORNEFF, J. Cancerogene Substanzen in Wasser und Boden. IV. Fütterungsversuche mit 3,4-Benzpyren und Detergentien. [**Carcinogenic Substances in Water and Soil. IV. Feeding Experiments with 3,4-Benzpyrene and Detergents**] *Arch. f. Hyg. u. Bakt.* 1960, June, v. 144, No. 4, 249–62, 2 figs. [46 refs.]

This paper is the fourth of a series on the problem of carcinogenic substances in water and soil [this *Bulletin,* 1959, v. 34, 1123; 1960, v. 35, 9]. There is a very detailed account of the nature and results of experiments on feeding mice with 3,4–benzpyrene with and without surface active agents. This work was undertaken because it is possible that even weakly acting carcinogenic agents, if ingested over a long period, might be dangerous. Hence the presence of detergents, mineral oil products and certain chemical industrial wastes in river water, which after treatment is to be used as drinking water, justifies increased attention and study.

The experimental mice were given a daily dose of 25 μgm. of benzpyrene for 400 days after which the presence or absence of hyperkeratosis, papilloma or carcinoma of the stomach was determined. The findings are fully discussed, and the most important of these was that definite carcinoma was produced only in the group of mice which had been fed with a normal diet, but had received benzpyrene in their drinking water to which detergent had been added. The groups of mice given either (1) dry food containing benzpyrene and drinking water containing 3% of detergent, or (2) the same dry food with benzpyrene and water without detergent, developed no carcinoma and had the same frequency of gastric pathological conditions such as papilloma.

It is considered that the use of detergents in the household is harmless, but that the solution of carcinogenic substances in waste waters and surface waters by detergents is conceivable. In the English summary the statement is made that "Drinking water obtained from river water has to be considered, for the present, injurious to health", but the original German says "possibly injurious". *M. E. Delafield*

MISCELLANEOUS DISEASES

GIBSON, H. B., HOWELER, J. F. & CLEMENTS, F. W. **Seasonal Epidemics of Endemic Goitre in Tasmania.** *Med. J. Australia.* 1960, June 4, v. 1, No. 23, 875–80, 2 figs.

In March 1949, a survey proved that endemic goitre was prevalent in most parts of Tasmania, and a recommendation was made that all children should be given 10 mgm. of potassium iodide in tablet form weekly. From the results of later surveys it was observed that there was a seasonal trend in the prevalence of visible thyroid enlargement. A special investigation was made at 3 schools, in 2 of which the children were given an increased dosage of 20 mgm. of iodide weekly, and in the third school the weekly dose remained at 10 mgm. Routine surveys were then made over a period of years either half-yearly or quarterly. A figure is given to show that in the period 1954–59 there have been 3 " substantial epidemics of epidemic goitre which occurred at about the same time each year. The peak incidence appears to be in late spring and summer, and the troughs occu in the autumn and winter ". The peaks, however, d not occur at exactly the same time each year. Th seasonal peak occurred in all 3 schools.

There is a description of the geography and climat of the locality in which the 3 schools are situated an of the economy of the district. The food supply an diet of the inhabitants are described. Tables give th incidence of various patterns of thyroid size in childre by sex and age.

In the summary it is stated " The same children appea to be affected each year, and they constitute some 30% of the children studied. In addition, it was noted tha approximately 18% of boys and 25% of girls had normal thyroid over the period of the study, and 29% of boys and 22% of girls had a constantly enlarge thyroid." There is discussion of the possibility that food goitrogen originating in weeds or fodder may b present in the milk at certain times and also that " su ceptibility to a food goitrogen is an inherent characteri tic of the children affected ". *M. E. Delafield*

MENTAL HEALTH

JONES, G. R., COCHRANE-DYET, E. M. & FULLER, A. M. **The Preventive Approach to Mental Retardation.** *Med. Officer.* 1959, Nov. 27, v. 102, No. 22, 277–83.

Prevention of mental retardation is likened to the treatment of the muscles of a fractured limb, for the latter early treatment can lead to almost complete restoration of function, and in the former early remedial measures may lead to substantially enhanced function of body and mind, whereas delay in both may lead to rigidity and inflexibility.

The health visitor can play an important part in early diagnosis, and the Backward Babies Clinic can then make a more certain diagnosis. Each baby can be assessed by the Ruth Griffiths method for development quotient, and also for complicating factors such as deafness and so on. According to the classification, appropriate remedial decisions can be taken, *e.g.*, those with low-grade mental deficiency can be sent to an institution, trainable defectives and those with suspected deafness can be sent to appropriate training units. The statistics of the Backward Babies Clinics for a period of 6 years are given.

Home training by an occupational therapist experienced in mental defective work is given during an interval before admission to an occupation centre or normal school entry. All this training tends to counteract the mother's tendency to continue to treat a handicapped infant as a baby, a process which, if unchecked, may go on for years.

The experience of the authors suggests that infants with an IQ of less than 20 should be admitted to a mental-defective institution as early as possible, those with an IQ between 20 and 29 can best be treated in a special clas room of an occupation centre and those with an IQ fro 30 to 39 are suitable for the occupation-centre worksho where they can learn enough to earn a modest livin Above this (IQ 40 to 49), training for unskilled work ar for simple intellectual tasks is practicable. Of tho initially suspected of mental retardation, only 20% w prove *bona fide* mental defectives and the remaind will be capable of fitting into the community at varyi levels of complexity. *H. G. Maule*

ROTH, M. **Mental Health Problems of Aging and th Aged.** *Bull. World Health Organization.* Genev 1959, v. 21, Nos. 4/5, 527–61. [Numerous refs.]

While much mental ill-health in old age may be part the unsolved problem of social integration, there are sti a number of specific disease processes present. Th paper attempts to provide a background against whic a new philosophy towards the aged might develop. reviews the mental health problems of the aged, settin them in their social, biological, medical and psychologic context. It discusses the possibilities of prevention an the application of existing knowledge to the ameliorati of illness.

Change in proportion of older people is due more t the reduction in birth rate than to the additional yea added to those who reach the age of 65.

The decline in mortality between the 17th and 19t centuries brought about the rapid increase in populatio —in Europe nearly 300%. Up to about 1900 the pr portion of young people remained fairly constant, b

since the end of the 19th century, with the falling birth rate, the proportion of young people has declined and that of older people has increased. In Europe, the increase in proportion of older people is more pronounced in industrial than in agricultural areas. In those countries in which the proportion of old people is less than in Great Britain, the proportion of dependent young persons is often substantially more, so that " dependants ", young and old, are a relatively larger proportion of the employed population.

Even where the proportion of old people is small, the total number may be large, and rapidly changing economic developments may have left them isolated and destitute.

Absence of sufficient data makes generalization of epidemiological aspects difficult. Some figures are available for the morbidity risk of senile psychosis in a few communities, but the difficulties of comparison are extensive. Trends may be indicated by hospital admission rates. Many studies show that admission rates to mental hospitals are disproportionately high for the elderly, but it is difficult to interpret this. It may or may not reflect a deterioration in the prospects of the old falling mentally ill. However, it would appear that the hazards of hospitalization with mental illness in old age is greater among the under-privileged members of the community; these people tend to be over-represented in urban communities, and a high proportion of them may be living alone. More detailed statistics of incidence of different disorders among different socio-economic groups are needed. Similarly, information is lacking about the (ill-)health of the elderly not living in institutions. Loneliness and emotional deprivation, which are common, are not in themselves mental illness, but they are problems of mental health. One main cause for the isolation of the aged may be changing cultural and social customs in communities of which they form a part.

The problem of suicide among the old is of special significance. Statistics are more objective and complete for this than for any other aspect of mental health in old age. Three factors—social isolation, a predisposition to respond to stress with psychiatric illness, and physical ill-health—seem to have great significance in suicide, but also have a relevance far beyond the confines of the suicide problem.

The causes of mental ill-health are discussed at some length. Deterioration which occurs after reproductive age cannot be eliminated genetically, and conditions which might, during the reproductive age, be selected out, will survive. There is still much to learn about the genetic influences, and important work in this field is quoted.

In considering some of the personality failures of old age, it is noted that these may form part of a continuous development, and the maladjusted personality of the aged may have its roots in adolescence or maturity.

Although existing knowledge in the social aspects of mental health in old age is steadily increasing, in few countries are the implications of this in terms of public health and social policy being taken seriously.

Where the social patterns lead to husband and wife both working, and to the decline in integration and size of the extended family the former role of the family may have to be taken over by the community. At the same time, a balance between family and community responsibility needs to be set.

The problem of prevention is equally a community problem in which public and private authority are both concerned. Housing and community planning has not always adequately considered kinship groups. Retirement pension policies may lead to economic dependance and psychological strain. The working potential and the optimum environmental conditions in which the elderly can work are only now being considered.

This comprehensive paper touches on all these problems, indicates the work that is now going on and provides an extensive list of references. The new knowledge that is currently being accumulated is faithfully reported. The implications of this new knowledge are set out. It is of special interest to note that many different workers, involved in different aspects of the problems of the aged, are converging on the same overall conclusion—that there is urgent need for a new social philosophy before it is too late. *H. G. Maule*

WILNER, D. M., WALKLEY, Rosabelle P., SCHRAM, J. M., PINKERTON, T. C. & TAYBACK, M. **Housing as an Environmental Factor in Mental Health: the Johns Hopkins Longitudinal Study.** *Amer. J. Pub. Health.* 1960, Jan., v. 50, No. 1, 55–63.

This report describes some of the preliminary findings in the field of social adjustment and mental health in an extensive longitudinal study of the effects of quality of housing on physical, social and mental health. A number of hypotheses had been formulated:—that slums have a generally bad physical effect, that certain specific diseases may be related to certain particular aspects of slum dwellings; that slums inhibit development of certain family and community relationships, and that slums inhibit certain aspects of personal psychological development. By interview and from public records information was obtained from an experimental group of 400 Negro slum families with 600 Negro families as control. The experimental group were under observation before and after rehousing. Some of the classical difficulties of such field surveys are mentioned. The technique used was to compare the responses of the two groups to the same questions at successive intervals of time and note the extent to which the differences within each group differed between the groups. As expected, big differences between the groups were recorded on attitudes and experience towards housing, *e.g.*, liking for their houses, safety for children's play and lack of space. There were also marked differences between the groups on social activities within the family and between families, the rehoused group showing a greater increase in these social activities. The architecture of the new housing, in many cases an 11-story block with communal corridors, lifts and play area, could be expected to facilitate such neighbourly contacts. Self estimation of social status showed some differences between the groups, but both groups equally regarded themselves as " going up in the world ".

Most of these scales are familiar to workers in this field. In examining psychological states a number of scales were specially constructed for this study. These

investigated mood, emotionality, optimism, morals, nervousness, and "potency" or efficacy of self-help. For none of these is significant differences between the two groups reported. It is possible that the time span of 18 months between "before" and "after" rehousing was insufficient for personal psychological states to be affected; and the next analysis 12 months later may show differences. The control group, who were not being rehoused, did actually have a high rate of housing movement into improved housing, thus the differences between the two groups was much less marked than had bee anticipated. Some of the implications of this are bein examined. *H. G. Maule*

WORLD HEALTH ORGANIZATION. PUB. HEALTH PAPER No. 2. **Epidemiological Methods in study o Mental Disorders.**

This book was reviewed on p. 625.

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation, Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

SCHYMA, D., GÄRTNER, H. & MOLL, G. Elektronenmikroskopische Untersuchungen über die Struktur eines neuartigen löslichen Ultrafilters zur Anreicherung von Bakterien aus dem Wasser. [**Electron-Microscopical Investigations of the Structure of a New Soluble Ultrafilter for the Concentration of Water-Bacteria**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 4, 562–7, 4 figs.

The authors have developed a soluble ultrafilter for use in the examination of water. The filter enables quantitative estimations of the micro-organisms present in a water sample and allows therefore an estimation of the true bacterial concentration in larger quantities of water. This mirco-filter has the following important characteristics, especially its ability to redissolve under physiological conditions.

The filter consists of aluminium alginate and forms a clear jelly approximately 0·5 mm. thick, which consists of 2 zones of different structures. (1) the primary gel membrane, a homogeneous layer only about 20 μ thick without any characteristic structure; (2) the capillary zone joined to it, in which the gel is pierced by round, parallel capillary tubes running into each other.

The primary gel membrane is therefore the sole deciding factor in the impermeability of the filter to bacteria, viruses and colloidal particles.

It seemed necessary that the structure of the membrane, which in the gel state only allows examination in broad outline with the light microscope, should be examined more accurately by means of dried preparations and electronmicroscopy to determine the pore size of the strata by means of test filtrates of colloidal gold.

The text is illustrated by 4 photographs showing the extent of penetration of the membrane by colloidal gold particles of different sizes. The previous assumption that the membrane will retain particles down to between 5–8 mμ in diameter is confirmed. *E. Windle Taylor*

DEL VECCHIO, V. & D'ARCA SIMONETTI, A. Il metod del Most Probable Number (M.P.N.), e la su importanza nella colimetria delle acque, con part colare riguardo a quelle destinate ad uso potabil [**The Method of the Most Probable Number an its Importance in Coliform Counts of Water wit Particular Reference to that intended for Potab Purposes**] *Nuovi Ann. d'Igiene e Microbiol.* 195 Nov.–Dec., v. 10, No. 6, 441–81, 1 graph. [30 refs

All values of the most probable number (MPN) shou not be taken in an absolute sense; normally a percenta error is always present in a greater or less degree, accor ing to the system followed for calculating the MPN. would really be desirable, at least in particular circun stances, to indicate for every value of MPN the corre ponding upper and lower limit values of the 95 confidence level.

The optimum series of dilutions that should be pr pared varies according to whether, in the samples water to be dealt with, the bacterial content is know even if only approximately, or quite unknown. In t first case it is advisable to prepare a set for identificatic or for setting out all inoculations in the same dilutio The amount of water to be inoculated varies—10 m 100 ml., etc., according to the initial level of the bacteri suspension, and must be chosen in such a way that eve quantity of inoculated water in each test should n contain on average more than one or two coliform In the second case, it is advisable for practical purpos to prepare more dilutions in orders of 10 (10 ml., 1 m 0·1 ml., etc.) so as to evaluate the 3 significant dilutio and to calculate the MPN. In the case of water intend for human consumption, in using the system of multip dilutions of the order of 10, it is always advisable inoculate a total quantity of water of not less than 2 to 250 ml.

The number of tests to be carried out when using mo

ilutions varies, and tables exist which permit the calulation of the MPN in various combinations. Generally, ne uses 3, 5 or 10 tubes for each dilution. The article ontains a comprehensive historical summary of the evelopment of the use of MPN up to and including 957, and indicates its limitations. Several tables for arious series are included derived from HOSKINS, WAROOP, WOODWARD and MCCRADY.

For a more precise appreciation of the coliform content f water intended for potable purposes, it is necessary o revise the conceptions which have hitherto regulated he significance of the presumptive test, and proceed to he isolation and the identification of the coliforms ventually present in whatever tubes become positive ndependently of the production of gas in the same nedium. *E. Windle Taylor*

HABS, H. & LANGELOH, U. Versuche über den Antagonismus zwischen *E. coli* und *E. freundii* bei der bakteriologischen Trinkwasseruntersuchung. [**Investigation of the Antagonism between *E. coli* and *E. freundii* in the Bacteriological Examination of Drinking Water**] *Arch. f. Hyg. u. Bakt.* 1960, June, v. 144, No. 4, 277–86.

Strains of *Escherichia coli* and *E. freundii* were noculated simultaneously into a glucose medium. Incubaon at 37°C. resulted usually in a preponderance of *E. coli* even when these organisms had been in the inority in the original inoculum. The antagonistic ctivity depended on the strength of the strain, thus the eakest of the *E. coli* strains examined was overgrown y the most active of the *E. freundii* strains. These findngs are discussed and the authors conclude that it is nlikely that a universal enrichment method will be found hich will fulfil the requirement of being selective for *E. coli* when these are sparsely present among other coliorm bacteria and at the same time allowing a good rowth of coliforms when *E. coli* is absent. It is therefore onsidered important in the examination of samples of rinking water to set up 2 batches of sugar cultures and o incubate one at 45°C. and the other at 37°C.
E. Windle Taylor

CHANG, S. L., BERG, G., CLARKE, N. A. & KABLER, P. W. **Survival, and Protection against Chlorination, of Human Enteric Pathogens in Free-Living Nematodes isolated from Water Supplies.** *Amer. J. Trop. Med. & Hyg.* 1960, Mar., v. 9, No. 2, 136–42.

Free-living nematodes have been found with some requency in some city water supplies in the United States nd also in trickling filters of municipal sewage-treatment lants. The authors had found that some of these ematodes fed readily in the laboratory on several types f coliform organisms and some preliminary experiments ad indicated that salmonellae and shigellae could surive in the worm gut for up to 4 days. Later, two nemaodes, *Diplogaster nudicapitatus* and *Cheilobus quadlabiatus* were cultured in the laboratory and adults and rvae were fed in different batches on *Salmonella typhi, alm. paratyphi, Salm. typhi-murium, Shigella sonnei, h. dysenteriae* II and examples of Coxsackie and ECHO nteroviruses.

It was found that the nematodes readily ingested plate cultures of the bacteria and fluid suspensions of the viruses. About 5–6% of the ingested typhoid and Sonne bacilli and about 12–16% of the paratyphoid bacilli and Coxsackie A9 virus survived for 24 hours in the gut of the worms, but after 48 hours the survivals were reduced to 0·1 and 1·0% respectively. There was no evidence of excretion by the worms of living pathogens. The nematodes were found to be highly resistant to the destructive action of free chlorine in the water and were unaffected by 120 minutes' exposure to 2·5–3·0 p.p.m. of chlorine. Even with an initial chlorine content as high as 95–100 p.p.m., 50–60% of the nematodes survived a 5-minute contact and 10–20% survived a 15-minute contact.

The ingested pathogens were so protected in the gut of the carrier nematodes that they had complete survival when 90% of the worms were immobilized by the free chlorine.

Although the majority of the ingested pathogens tend to disappear after 1–2 days a significant proportion may remain viable if the worms are carried from their normal habitat to water supplies within 24 hours and they will survive routine chlorination as practised in the field. It is concluded, therefore, that nematodes of the Rhabiditidae family of sewage-treatment origin may be potential carriers of human enteric bacteria and viruses.
H. J. Bensted

DICK, E. C., SHULL, I. F. & ARMSTRONG, A. S. **Surface-Subsurface Distribution of Bacteria in Swimming Pools—Field Studies.** *Amer. J. Pub. Health.* 1960, May, v. 50, No. 5, 689–95.

As a result of the suggestion that bacteria tend to become concentrated on the surface of swimming pools, an investigation was made of surface films in Kansas pools.

The results of examination of 7 pools showed some degree of concentration of bacteria but not to any alarming extent. Almost all average surface or subsurface counts fell within the standards of the American Public Health Association for a "fair" quality swimming pool (between 200 and 1,000 bacteria per millilitre).

It was noted, however, throughout the study that the predominant organisms on the plates were from the upper respiratory tract, often in clumps and resistant to chlorine. The use of blood agar plates is suggested as being informative of the sanitary condition of swimming pool water. *E. Windle Taylor*

SCHWEISFURTH, R. & ZIMMERMANN, W. Untersuchungen über die Einwirkung von Kraftstoffen auf Wasser und Boden. I. Versuche zur Entwicklung von Laboratoriumsmodellen. [**Investigations of the Action of Fuel-Oils on Water and Soil. I. The Development of Small-Scale Laboratory Models**] *Arch. f. Hyg. u. Bakt.* 1960, July, v. 144, No. 5, 411–20, 7 figs. [12 refs.]

The increasing use in the last decades of mineral oil products and similar substances for power purposes has resulted in a much greater risk of these materials reaching the soil in various ways and hence polluting the ground

water. These dangers are described at some length and there follows a detailed description of apparatus set up in the laboratory for the study of the bacteriological and chemical effects of the addition of chemical fuels to soil and water. There are photographs of the apparatus and details of the experimental results.

The main observations in these experiments were th the addition of even small amounts of a commerc petrol to a large volume of soil brought about an increa in the total numbers of bacteria, an enrichment of ce tain bacterial species and a diminution in the nitra concentration. *M. E. Delafield*

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

DEPT. SCIENT. & INDUST. RES. **Water Pollution Research 1959. The Report of the Water Pollution Research Board** [GARNER, F. H., Chairman] **with the Report of the Director of the Water Pollution Research Laboratory** [SOUTHGATE, B. A.]. pp. vi + 115, 60 figs. & 4. pls. [Refs. in footnotes.] 1960. London: H.M. Stationery Office. [7s.]

In this volume there is first a short report of the Water Pollution Research Board in which it is stated that as the type of work undertaken by the Research Laboratory is becoming of steadily increasing importance in the national economy, an increase in laboratory staff and extension of laboratory space is needed. Plans for a new wing to the Laboratory are well advanced.

The Report of the Director of the Water Pollution Research Laboratory contains interesting accounts of continuing and new researches. The section on Basic Processes for the Treatment of Polluting Liquids contains sub-sections on experiments of different types on:—(1) aeration in the activated-sludge process, (2) the relative merits of clinker, blast furnace slag, broken rock and rounded gravel as media in percolating filters, (3) use of a radioactive tracer for measuring retention characteristics of a percolating filter, (4) effect of synthetic detergents on the nature and amount of sewage sludge, (5) dewatering of sludges, and (6) respiration of living films of organisms in the treatment of sewage.

Work on industrial waste waters included experiments on the treatment of meat-processing wastes, waste waters containing (1) cyanide and (2) cyanide and chromate, coke oven effluents, tannery wastes, wool-scouring liquors and farm wastes.

An interesting part of the section on sewage research is the reference to the new type of surface-active material, an account of which was given in the Report for 19 [this *Bulletin*, 1959, v. 34, 915] and to the "Luton expe ment" (also described elsewhere) in which the detergen used in the town were replaced by the new material order to compare the effects of the 2 materials on sewa purification.

In other sections there are descriptions of the ma pieces of work which have been done on (1) the effec of various types of pollution on fish, (2) chemical a biological conditions in fresh-water streams, and (3) t survey of the River Thames.

The last part of the report is on certain new or im proved instruments and methods: (1) recorder f suspended solids in sewage effluents, (2) indicator of t total number of air bubbles leaving a submerged orifi (3) dissolved oxygen indicator, (4) solar radiation record (5) automatic anti-coincidence counter, (6) automa sampler and (7) radiochemical analysis of samples water, aquatic vegetation and mud. *M. E. Delafield*

WATER POLLUTION CONTROL FED. RES. COMMITT [HEUKELEKIAN, H., Chairman]. **A Review of t Literature of 1959 on Wastewater and Wat Pollution Control.** *J. Water Pollution Control Fe* 1960, May, June & July, v. 32, Nos. 5, 6 & 7, 44 81; 545–93; 681–720. [Numerous refs.]

MOORE, B. **Sewage Contamination of Bathing Beache** *Roy. Soc. Health J.* 1960, May–June, v. 80, No. 183–7. Discussion 187–9.

A general account of recent British work, see t *Bulletin*, 1960, v. 35, 635.

INFESTATION

MAGUIRE, H. C., Jr. & KLIGMAN, A. M., with the technical assistance of Margaret HEINEMAN. **Norwegian Scabies.** *Arch. Dermat.* 1960, July, v. 82, No. 1, 62–4, 2 figs.

There are only 10 cases of Norwegian scabies reported in the American literature. Most cases occur in institutions, particularly among patients with neurological or mental disorders, mongols being particularly predisposed. Clinically it presents as crusted hyperkeratoses of t palms and soles, sometimes large enough to interfe with normal movement. Oozing may be a disagreeab feature. There are often enormously thickened nails d to massing of horny material under the nail plate. El where are hyperkeratotic lesions distributed fai symmetrically over the body. The lesions of ordina scabies may also be present on the usual sites; itchi however, is usually not prominent.

Microscopically, the horny layer is greatly thickened ith innumerable multistoried tunnels which are the past present dwelling places of all stages of the sarcoptic ite. There may be as many as 2 million adult mites the crust from a single case. The mite is the same that which causes ordinary scabies and the peculiar haracteristics of the disorder are entirely due to a unique sponse on the part of the host.

4 cases are reported in patients aged 16, 23, 24 and 42. ll were male mongols in an institution. There was at is time a marked increase in the number of cases of dinary scabies.

Treatment consisted of a week of daily soaks and rubs followed by the application of 25% benzylbenzoate in tincture of green soap, then followed 4 weeks of daily inunctions of 4% sulphur ointment to all lesions. By that time the disease was clinically cured and there were no relapses. The isolation and treatment of these 4 patients was followed by a sharp decline in cases of ordinary scabies at the institution.

The authors stress the need for a careful search for one of these cases in an institution where there is an unexplained endemic of ordinary scabies. The diagnosis should be considered in any case showing hyperkeratotic, crusted eruptions on palms and soles. Microscopic examination of scrapings of horny material will always show the presence of mites in Norwegian scabies.

H. T. H. Wilson

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

ITTING, E. Sicherheitsmassnahmen für die Schutzgasschweissung. [**Security Measures for Shielded Gas Welding**] *Zent f. Arbeitsmed. u. Arbeitsschutz.* 1960, June, v. 10, No. 6, 129–34, 3 figs.

Shielded gas welding is the name given to a special rm of arc welding in which electrode, arc and molten etal are enclosed in a concentric stream of gas, thereby eventing escape of oxygen and nitrogen into the rrounding atmosphere. The two principal forms of is process are the Wolfram Inert Gas (WIG) or argon c welding, and Metal Inert Gas (MIG or SIGMA).

In the argon arc apparatus the arc is placed between e Wolfram electrode and the welding point, while the lding material is held in the left hand. In SIGMA lding the arc is placed between the welding point and mechanical automatic electrode and the burning and eed of appliance of the electrode wire are kept constant d melting continuous. These methods eliminate the ief hazards of the usual methods of welding—electric ock, sparks, fire, etc.

Argon carries no special health hazard but care is eded when CO_2, either pure or mixed with argon or ygen, is used.

Both processes produce the maximum amount of ultraolet radiation, and the ozone arising from its action the arc, causing symptoms in a welder using the GMA apparatus, was found to be 9 times the nonxic level. Oxidation of Wolfram electrodes, which ay contain 2% of thorium oxide, may occur if the gon stream is turned off too soon after completion of lding; the wolfram oxide so formed may cause mucous embrane and gastric irritation. Modern argon arc tallations are provided with means of continuing the gon stream for about 15 seconds after cessation of lding.

Carbon dioxide has recently been used as a shielding gas in SIGMA welding of carbon steels. Some of it is decomposed into CO and O_2. At 10 cm. distance from the arc, with no exhaust ventilation, concentrations of 0·02% of CO have been found, while in a closed room of 60 cubic metres capacity the CO level reached in 2 hours was 0·02% and that of CO_2 1·2%.

Argon arc cutting of aluminium and copper is carried out with a mixture of argon and hydrogen, and of high alloy steels with nitrogen with a small amount of argon. Special care is needed in welding alloys containing cadmium, beryllium, zinc, copper, lead, aluminium and silica.

Escape of hydrogen into a closed room carries a potential explosive hazard. Formation of nitrous oxide can be avoided by using 99·98% pure nitrogen. The vapour arising from argon–arc cutting should be directed away from the worker. Suitable exhaust ventilation apparatus and respiration filters are described in detail and illustrated diagramatically. *E. Browning*

BORNEFF, J. & BARTHELMESS, G. Über die Entstehung der Berufskatarakte. [**The Formation of Occupational Cataract**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 414–24, 3 figs. [15 refs.]

This paper with its long description and discussion of experimental findings is based on the examination of 10 human lenses, the degree of opacity of which had been clinically determined before they were surgically removed for a variety of conditions. The lenses were examined against air and against water by spectrophotometer (Zeiss–Spektralphotometer PMQ II – wave length range 600–2,500 mμ).

The results were that absorption of ultra-red rays is

determined by the water content of the lens, for water-free lens constituents are more permeable to these rays than water. Special reactions in the lens fibres to radiation are therefore unlikely. These findings taken in conjunction with those of other authors point to the conclusion that occupational cataract is to be regarded as a disturbance of the development of the germinal lens epithelium caused by damage to the equatorial zone.

M. E. Delafield

LOVELESS, N. E. **The Development of Rotary Nystagmus in the Cat as a Function of Age.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 46–51, 3 figs. [29 refs.]

It is known that the onset of miners' nystagmus is related to the age of the miner. It is a disease of middle-age commonly occurring after some 20 to 30 years' underground work. The difficulties of controlling many of the factors which appear important in the occurrence of nystagmus led to an experiment in cats designed to investigate the effects of age. 35 cats were kept in darkness and regularly examined for oscillation of the eyeballs. Every animal showed oscillation and the age of the animal was found to be related to the rate of increase of amplitude of oscillation.

The possible implications in relation to the age at which miners should start underground and the importance of illumination in underground work are discussed as well as the intricate psychological factors which have been associated with oscillation. *H. G. Maule*

ANDA, B. Forekomsten av vasopastiske forstyrrelser (" hvite fingrer ") blant gruvearbeidere i Sulitjelma. [**Incidence of Vasopastic Disturbances of Hands in Miners**] *Nordisk Hyg. Tidskr.* 1960, v. 41, Nos. 5/6, 123–47, 8 figs. [35 refs.]

The English summary appended to the paper is as follows:—

" 118 miners exposed to vibrations from vibrating tools at Sulitjelma Coppermines in Norway have been examined with regard to ' white fingers.'

" 71 out of 85 drillers operating drills with 3,000–4,000 vibrations per minute, had ' white fingers.' The average time of exposure before onset of symptoms was 5 years. X-ray examinations revealed pathologic changes in bones and joints of the hands in 37 cases; in addition traumatic osteoarthritis in the elbow (6 cases) and in the shoulder (1 case). On the basis of their complaints and especially of the results of the clinical examinations, the subjects have been classified into 4 groups. Normal: 14. Stadi I: 35. Stadium II: 17. Stadium III: 19.

" Examinations of the remaining 33 miners sho that 32 had ' white fingers.' 21 of them had at an ear period of time been exposed to work with pneum tools as drillers.

" The prophylactic measures are discussed."

BROADBENT, D. E. & LITTLE, E. A. J. **Effects of No Reduction in a Work Situation.** *Occupatio Psychology.* 1960, Apr., v. 34, No. 2, 133–40.

Many laboratory studies on the effects of noise h shown that, for tasks that are long and require const attention, there may be a decline in performance. T effect is rather to increase the frequency of moment lapses in efficiency and appears only with noises of m than 90 decibels.

The study here described was carried out among gro of factory workers performing standard tasks in production of cinefilm in their normal working con tions, except that, for the experiment the effects reduced noise levels were examined. One room w treated by placing sound-absorbent material on the w reducing noise level from about 99 db to 89 db. Vari measures of working efficiency were adopted, *e.g.*, measurement of rate of work during periods of no st page (Point hour), number of shut-downs of proc number of occasions of broken work, number of c for maintenance, time occupied for curing maintena faults, labour turnover, and absence from work.

The results showed that for many of these crite there were significant changes after the noise reducti However, the improvements were not always confined the workers in the acoustically treated rooms. Po hour, for example, improved in the experimental and the control group, which might be accounted for b general improvement in morale and attitude to wo Broken work (if due to the operator) on the other ha declined significantly more in the treated than in untreated room.

Calls for maintenance and time occupied by stoppa for maintenance did not show any statistically signific change. Neither labour turnover nor absenteeism sho significant difference except that for the latter both gro of experimental workers showed some slight advant compared with the remainder of the department.

When comparing these studies with those (m commonly) undertaken in experimental laboratories, t facts must be remembered: First, this study deals w a " real-life " situation, and second, the experiment tended over 2 years and involved a series of 4 periods 6 weeks' work each. *H. G. Maul*

OCCUPATIONAL PHYSIOLOGY

ION, Judith S. **A Comparison of the Emotional Stability of Coal-Miners and Railwaymen.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 41–5, 2 figs. [11 refs.]

Two groups of men, 67 coal-face miners and 50 mis-ellaneous railway workers, were given various tests esigned to measure emotional stability. 3 tests showed gnificant differences between the groups. HERON'S notional instability personality inventory (*Brit. J. Psy-iology*, 1956, v. 47, 243) suggested that miners are more nstable than railway workers, though the author thought e difference might be largely accounted for by the iners' greater preoccupation with their health. In nother test (EYSENCK'S fluency; *Dimensions of Person-ality*, London, 1947, Kegan Paul) the miners obtained more neurotic scores than the railwaymen.

It has been suggested that the stress of daily working conditions in the mines is greater than that in most other occupations. Despite the difficulties of finding tests which are sensitive to emotional stability but not to other personality traits there may be a real difference between the stability of miners and that of other workers.

H. G. Maule

KNOWLES, J. H. **Respiratory Physiology and its Clinical Application.**

This book was reviewed on p. 947.

OCCUPATIONAL DISEASES

AVRÁTIL, M. Der Einfluss des Grubenstaubes auf die Entwicklung der chronischen asthmoidalen Bronchitis. [**Influence of Mine Dust on the Development of Chronic Asthmatic Bronchitis**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 17, No. 6, 618–26, 3 figs. [16 refs.]

109 iron-ore miners who had worked for more than years underground were studied clinically and physio-gically, by measuring the Forced Expiratory Volume EV) and by pneumotachography. Comparison of the eumotachograph results in 24 patients with asthmatic onchitis and 29 normal controls showed that the miners reed closely with the normal controls but differed gnificantly from the patients.

95 of the miners were examined again after a shift derground. Signs of bronchitis (increased expiration d dry rhonchi) were heard in twice as many men as the previous occasion. [It is not stated if the same server auscultated on the two occasions.] The vital pacity was higher in 32, lower in 10 and the same in of the men; while the FEV was higher in 8, lower 46 and the same in 41. The author concludes that ese studies do not support a bronchospastic influence dust; but that they indicate that dust induces an itative bronchitis.

The conclusions apply only to iron-ore miners. Further udies on these lines are at present being carried out coal workers.

I. T. T. Higgins

VRIES, K., ORIE, N. G. M. & MEY, A. V. M. **Asthmatic Factors in Chest Complaints of Miners.** *Acta Med. Scandinavica.* 1960, July 15, v. 167, No. 4, 301–8, 1 fig. [23 refs.]

The disproportion between the symptoms and the radio-gical findings in miners with chest complaints suggests at another factor is involved. This factor may be an hmatic disposition evidenced by various symptoms which have common features such as familial incidence, eosinophil cells in the blood, bronchospasm, etc.

A hereditary mechanism of this type could be used to distinguish between chest complaints of miners with asthmatic predisposition and those due to dust. School-children in an area in the Netherlands who had this asthmatic predisposition as evidenced by slight or severe asthma or chronic relapsing bronchitis were selected and a comparison group taken from their schoolmates. The male family relatives were traced and those who were miners were studied as regards chest complaints, X-ray findings, etc. It was found that the number of days of disability due to dyspnoea or other chest conditions was greater in the asthmatic group than in the control group. It was also higher in the underground workers than in the surface workers. There is therefore an additional factor inherent in working in an underground environment. No significant difference was found in the radiological findings.

Charles L. Sutherland

BASTENIER, H., ASSOIGNON, L., DESLYPERE, P. & DE GRAEF-MILLET. Les images radiographiques d'agrandissement direct dans la diagnostic des pneumoconioses. [**Macroradiography in the Diagnosis of Pneumoconiosis**] *Bruxelles-Méd.* 1960, June 19, v. 40, No. 25, 893–903, 6 figs.

Macroradiographic films are being studied in Belgium with a view to their use in the diagnosis of pneumoconiosis. The technique is given in detail. In brief, it involves the use of a fine focus tube 0·3 x 0·3 mm., films of 35 x 35 cm., allowing a view of 7 to 8 anterior intercostal spaces, and an exposure of 0·10 to 0·15 seconds. The amperage is not above 25 milli-amperes and the kilovoltage between 72 and 86 for an adult. The patient is placed at 35 cm. from the film and the film is taken at a distance of 1 metre.

By this method small nodules are shown up clearly

and enlarged; superimposed shadows are separated. The diagnostic points are:—

(1) 7 anterior intercostal spaces throughout their length, should be visible on the film.
(2) at least 10 nodular shadows should be visible in each interspace;
(3) the distribution should be bilateral.

To test the value of these criteria a group of persons who had no dust exposure were examined both by macroradiograph and the ordinary method. The standard film was normal in most cases but some showed fibrosis. The magnified film showed a few nodules only. A second group who had been exposed to silica dust fell into two types. One showed a more or less definite linear marking on the standard film, but macroradiographically none or a few nodular shadows. In this type, a claim for compensation would be dismissed. In the second type the PA film showed accentuated linear marking with doubtful "pinhead" nodular shadows. The macroradiograph proved useful in deciding such cases.

Pictures of films are shown but these are of doubtful value to the reader. In the summary it is stated that details of method and interpretation of results have to be established. *Charles L. Sutherland*

VALENTIN, H., LICHIUS, N. & ZERLETT, G. Über das Verhalten der Lipoproteide und Proteine des Blutserums bei der Silikose. **[Serum Lipoprotein and Protein Contest in Silicosis]** *Arch. f. Gewerbepath u. Gewerbehyg.* 1959, v. 17, No. 3, 227–37, 3 figs. [Numerous refs.]

The authors made a detailed study of the serum protein and serum lipoprotein electrophoretic patterns of 56 silicotic patients. The results confirmed those of previous workers in that serum albumin was in the main decreased whereas gamma-globulin was increased; lipoid fraction I levels were on the whole lower than those found in healthy subjects. There was no relation of serum lipoprotein content to grade of severity of silicosis. *D. Rivers*

NICOD, J. L. & GARDIOL, D. La silicose dans la moelle osseuse. **[Silicosis of the Bone Marrow]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 1, 79–90, 12 figs. [19 refs.]

Silica dust in the lung produces lesions which always start as an accumulation of histiocytes round little blood vessels. Some particles are carried *via* the reticuloendothelial system, to other organs, and such particles retain their pathogenicity. The presence of silicotic nodules in the liver and spleen is a common finding in the silicosis of miners and industrial workers in Switzerland, but the presence of silicotic changes in the bone marrow has not so far been clearly demonstrated. Nicod and Gardiol think that the reason for this is that the morphological study has not been sufficiently complete. They have therefore examined the vertebral and femoral bone marrow from all silicotic cases examined post mortem over a period of years, and have traced the progress of lesions caused by silica. The first reaction is an accumulation of histiocytes, at first fluffy, then mo discrete. Silver staining shows up a close meshed n work of fibres. Although such lesions become mo sharply defined they mostly do not progress further. this stage they are indistinguishable from those produc by infections such as tuberculosis. That is why they ha been ignored by others interested in silicosis.

In the case of a miner lesions similar to silicosis we found. One nodule was visible to the naked eye, and the middle of this nodule were collagenous fibres, a peripherally reticular fibres. The polarizing microscc revealed, towards the centre of the nodule, bi-refring crystalline particles. Illustrations are given of the varic stages of the disease in this patient. In other cases was found that the silicotic lesion commences as a c of histiocytes round blood vessels. This shows up in femoral marrow which is poor in cells. The tubercul focus can be distinguished from the silicotic lesion; has no central vessel; it has epithelioid cells and gi cells.

It is concluded that the presence of silicotic nodules the bone marrow shows that silica retains its toxic even when it leaves the lung. Silicotic lesions sho therefore be found in still more organs. Finally, morphological study does not give any lead as rega functional damage. *Charles L. Sutherlanc*

SARTORELLI, E. & SCOTTI, P. Ricerche sull'azione bro codilatatrice di farmaci ganglioplegici e vagoli in enfisematosi e silicotici con bronchite asma forme. **[Studies on the Bronco-dilating Action Ganglioplegic and Vagolytic Drugs in Empl sematous and Silicotic Patients with Asthma Bronchitis]** *Med. d. Lavoro.* 1960, Mar., v. No. 3, 174–82. [25 refs.]

The English summary appended to the paper is follows:—

"A study was carried out on the bronchodilat action of vagolytic drugs: 'Prantal' (N.N dimethyl piperidylidene-1,1-diphenylmethane-methyl-sulphate) a 'Esentil' (Beta - diethylaminoethyl - 1 - ciclohexyl - cyc hexane carboxylate hydrocloride), and on three gang plegic drugs: promazine, chlorpromazine and laevop mazine. The drugs were studied on 54 patients w chronic asthmatic bronchitis associated in 34 cases w pulmonary emphysema and in 20 cases with a vary degree of silicosis. The bronchodilating effect of th drugs were evaluated by means of spyrographic tests basal conditions and after 15', 30', 40' and 60' from administration of the drugs by one or more routes (inu venous, intramuscular, aerosol). In every patient one more pharmacodynamic control tests were perform (intravenous aminophyllin; intramuscular adrena aerosol isopropylnoradrenalin). A total of 851 spy graphic tests were carried out.

"The results show that both tested vagolytic dr have a bronchodilating activity, which is higher 'Prantal' (37·5 mg. by intramuscular route, as compa with 10 mg. 'Esentil' by intravenous route or by aeros

"At the observed conditions of dose and route administration, both the vagolyting drugs induced secondary symptoms.

"The tested ganglioplegic drugs also showed a bronhodilating activity, almost of the same degree for the ested drugs, at the same dose level (25 mg.) and route f administration.

"The bronchodilating effect was very marked after ntravenous administration of promazine, chlorpromazine nd laevopromazine, moderate after intramuscular admin-tration of promazine and chlorpromazine and after erosol administration of promazine. At the observed ose levels intravenous chlorpromazine was always badly olerated and both promazine by intravenous and aerosol dministration, and chlorpromazine by intramuscular oute, induced some secondary disturbances in some atients. Intravenous laevopromazine and intramuscular romazine were well tolerated.

"Considering bronchodilating activity of the drugs nd the patients' tolerance, it is concluded that 'Prantal' nd promazine by intramuscular administration and evopromazine by intravenous administration can find useful application to the treatment of bronchospastic ndromes which are frequently associated with chronic ng diseases".

LMER, G. Thoraxchirurgische Behandlung von Staublungenkranken. Erste Erfahrungen an 62 Fällen der Schweizerischen Unfallversicherungsanstalt. [**Surgical Treatment of Pneumoconiosis**] Reprinted from *Helvetica Chirurgica Acta.* 1960, v. 27, No. 2, 117–80, 21 figs. [31 refs.]

The unsatisfactory results of conservative medical eatment of silicosis and silicosis with tuberculosis has d the medical staff of the Swiss Accident Insurance stitution to examine the results of surgical intervention. his is an account of 62 insured workers who have had rgical treatment for their lung condition over the period 51 to the end of 1958.

The indications for surgery in these cases depended on factors:—(1) Degree and extent of the silicosis, (2) ype and spread of the tuberculosis, and (3) Degree of npairment of respiratory functions and of the circulation. Simple silicosis is rarely an indication for operative terference, but a superadded localized tuberculosis or spicion of tumour would be. The most favourable nditions for resection are diseases limited to one lobe, ch as an isolated cavity or a tuberculoma. The general inciples for operations on silicotics are those laid down r tuberculosis itself, but greater care has to be taken bronchial conditions to avoid postoperative bronchial tula. Antituberculosis treatment was carried out in l cases to stabilize the tuberculosis. The respiratory nction and the cardiac condition were investigated in tail from the clinical and physiological standpoints. carefully chosen cases there is no fear that silicosis d its effects will lead, after operation, to increased spnoea and overloading of the right heart. Lobectomy as considered the operation of choice in silicotuberlosis; the presence of silicosis does not greatly increase e risk. The risks in the operation were (1) development bronchial fistula, (2) incomplete expansion of the rest the lung, (3) atelectasis of remaining lung, (4) respiry or cardiac insufficiency (rare).

The surgery assisted diagnosis. By examination of the specimens removed, 6 cases were shown to be tuberculosis *per se*, and in 5 cases suspected of tumour the fear was dispelled by histology. In all, there were 18 deaths in the 62 cases; 7 occurred during or immediately after operation. The post-operative progress of the other patients cannot be completely assessed because of the limited time since operation. A few are on full work but the chief benefit claimed for lobectomy is that it makes the sputum free of tubercle bacilli.

Two points arise from this paper. In Great Britain pneumoconiosis is taken to be a contraindication for chest surgery: the risk seems to be overrated. Secondly, pneumoconiosis accompanied by tuberculosis attracts the same benefit as pneumoconiosis itself under our Insurance Act but in Switzerland if the tuberculosis is quite separate from a minor degree of silicosis, no compensation may be payable.

Charles L. Sutherland

STURM, W. Über die prophylaktische Anwendung von Flüssigkeitsaerosolen in Staubbetrieben. [**The Prophylactic Use of Fluid Aerosols in Dusty Trades**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, June, v. 6, No. 6, 333–8. [22 refs.]

The author believes that the inhalation of inert dust damages the lungs. Every means should be used to prevent the inhalation of such dusts equally with those causing pneumoconiosis. Complete removal of the danger of dust inhalation cannot always be achieved.

For some years the use of aerosols has held the centre of interest in combating the effects of dust inhalation. The properties of a fluid aerosol are described. The particles are of about 0·001–5·0 microns and their action depends on their size, number, electric charge and chemical composition. If a fluid aerosol is added to a dust cloud, the unequal size of the particles leads to coagulation, to increased size, and so to lessened entrance to the lung.

The reasons for the use of calcium chloride solution in aerosol form to prevent the consequences of dust inhalation are, among other things, that is diminishes secretion, stimulates phagocytosis, limits allergic reaction and promotes the cleansing function of the lung. Natural calcium chloride springs occur in the central highlands of Germany; these are used in the treatment of bronchial asthma and other affections of the air passages. At Bad Suderode treatment of dust disease is carried out by aerosol inhalation of this water. At Schmalkalden there is planned an extension of these facilities for the prevention and treatment of bronchitis in workers exposed to dust.

Several of the larger works have set up plants for aerosol prophylactic treatment for workers in dust. All workers should be obliged to undergo the treatment; for example the treatment centre in coal mines should be between the changing room and the washroom. Suitable arrangements for smaller firms are described. Advice on the erection of suitable plant is given by the Physical Department of the Institute for Occupational Hygiene in Berlin-Lichtenburg. The treatment, when set up, requires constant medical guidance and supervision.

Charles L. Sutherland

MÜLLER, H. A. Zur pathologischen Anatomie der Talkumlunge. [**The Pathological Anatomy of Talc Lungs**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 262–82, 9 figs. [54 refs.]

The author describes in detail the macroscopic and histological appearances of talc lesions in the lungs of 2 men. Both had been exposed for many years to talc dust in the same gum factory. The specimen from the first case was provided by surgical biopsy during thoracotomy and that from the second by lobectomy performed to remove a drug-resistant cavitated tuberculous lesion. With minor exceptions, the talc lesions from both patients showed the characteristic features of talc granulomata as described by SCHEPERS and DURKAN [see this *Bulletin,* 1956, v. 31, 36 *bis,* 38]. *D. Rivers*

KUHNE, W. Die Morphologie der Schmalkaldener Schleiferlunge. [**Morphology of Grinders' Lung in Schmalkalden**] *Arch. f. Gewerbepath u. Gewerbehyg.* 1960, v. 18, No. 1, 37–52, 8 figs. [25 refs.]

In the neighbourhood of the market town of Schmalkalden on the south of the Thüringer Forest the manufacture of tools, such as drills, spanners, pliers, etc., is carried on. In addition to large factories there is a multitude of small works where work is carried out under very unfavourable conditions. Artificial wheels, corundum, emery or carborundum are used. The dust raised in the process consists largely of iron oxide, Fe_2O_3, with traces of other metals and the main constituent of the stones and the binding material.

The material for this report came from the post-mortem examinations of 9 grinders between the ages of 54 and 69 years. In 2 cases death was caused directly by the pulmonary condition. One of these showed simple nodular silicosis, the result of a 5-year spell using natural sandstone. The dust of the stones in use does not produce silicosis.

Emphysema was found in all the lungs but in more than half the cases it was of the bullous type. Chronic bronchitis was also found in all cases although it was obscured by terminal infections. Deposits of dust (mostly carbon and iron oxide) were found in the pervascular, peribronchial and pleural lymphatics. In seven cases changes were found in the blood vessel walls possibly leading to pulmonary hypertension.

There are 8 illustrations of the naked eye and microscopic appearances, and the possible connexion between bronchitis, emphysema and deposition of dust is discussed at length. The fibrosis present however is not limited to the neighbourhood of the dust deposits.

In general the pathological findings in these cases, apart from the silicosis case, do not differ, or only in extent, from those observed in other lungs. The position of dust in relation to these changes requires further investigation and comparison with findings in a similar group with no occupational dust exposure.

Charles L. Sutherland

JENNY, M., BÄTTIG, K., HORISBERGER, B., HAVAS, L. GRANDJEAN, E. Arbeitsmedizinische Untersuchu in Zementfabriken. [**Occupational Medical Inves gation in Cement Works**] *Schweiz. med. Wo* 1960, June 25, v. 90, No. 26, 705–9, 5 figs. [25 ref

This is the first systematic investigation in Switz land into the possibility of respiratory complai arising from the inhalation of cement dust. No f silica is present in Swiss cement, so silicosis is not risk, a fact confirmed by the radiological examinati of some of the workers. In all, 488 employees at factories were studied.

The absentee rate at one of the factories was mu higher than at others; the percentage of men complai ing of cough and of those with sputum was also high in this factory. The cause of this might be partly d to social factors, epidemics, etc. A study of smoki habits shows that exposure to cement dust does n increase coughing in smokers. It is sugested that tho who are resistant to smoker's cough are also resista to dust. The non-smokers show a surprisingly hi proportion with chronic cough as compared with t figures given by another author. Perhaps a better co parison would have been with a non-occupational gro studied by the authors themselves. However, it is co cluded that this shows that cement dust is irritating the respiratory passages.

The physical signs found did not lead to any defin conclusion. The vital capacity was not influenced the length of dust exposure. In a few workers t maximum expiratory force was reduced.

An attempt was made to relate the findings to t intensity of exposure by dividing the workers into groups. The 2 groups most exposed to dust show a tendency to increased pathological signs, but t difference was not statistically significant.

Charles L. Sutherlan

INTERNAT. UNION OF PURE & APPLIED CHEM. Appli Chem. Sect. Toxicol. & Indust. Hyg. Divisio **Methods for the Determination of Toxic Su stances in Air** [GAGE, J. C., STRAFFORD, N. & TE HAUT, R. (Prepared by)]. Loose-leaf pp., illustrate 1959. London: Butterworths Scientific Publicatio [30s.]

This loose-leaf publication gives details of metho for the determination of 21 of the more important a dangerous toxic substances which may occur industrial atmospheres.

In an introductory section reference is made to t considerations which influenced the choice of t methods adopted. The methods must be sensit enough, so that before a method for a particular co taminant can be selected the degree of sensitivity th is required must be known. To this end, the Divisi has examined the toxicological and clinical eviden and has defined the concentrations which should n be exceeded where men are continuously exposed f 8 hours each day. In the text describing the methods

determination of individual contaminants these maximum allowable concentrations are stated, and the methods are sensitive enough to measure those concentrations.

Ideally, the methods should be so simple as not to require elaborate apparatus or the services of a skilled analyst. Hence, complicated methods many of which provide high sensitivity, specificity and accuracy have been rejected. But simplicity should not be gained too much at the expense of specificity and precision. It is rarely necessary that quantitative results with a precision greater than 20% are needed, but an acceptable degree of precision must be attainable at the maximum allowable concentration, however low this figure may be. It has not been possible in every case to find a method which conforms to all these guiding principles. For some substances 2 methods have been selected; a simple and rapid but not very precise procedure which will give a warning of excessive concentrations, and a more complex one which can give more reliable results.

There is a valuable discussion of the procedure for investigating a factory atmosphere; of where, when, how often and for how long the tests must be made so that a reliable estimate of the hazard is obtained. When men are exposed to fluctuating concentrations a detailed knowledge of the toxicological properties of the contaminant is necessary to decide whether the mean concentration over a prolonged period gives a reliable measure of the hazard. Generally a series of short-period samples will give a more complete picture.

In most of the methods adopted a measured volume of air is drawn through a liquid capable of retaining the toxic substance in an absorber or bubbler. The concentration of the substance in the liquid is then determined, preferably colorimetrically, although in some instances titration is necessary. In other methods the air sample is drawn through paper or granules impregnated with reagents, and the concentration is determined directly from the colour produced.

There is a very useful section on the collection of the air sample by means of a hand pump, water aspirator, evacuated vessel, or continuous pump. Liquid absorbers and bubblers, and solid absorbers, for the extraction of gases and vapours are described A discussion of the extraction of particulate matter from the air sample is limited to methods for the determination of the total dust weight concentration, and the midget impinger or filter paper may be used for this purpose. Finally in this introductory material, the quantitative determination of the toxic substance in the air sample is dealt with.

The methods of determination of individual substances are then described in a series of leaflets. Each gives the principle of the method employed, with a mention of the maximum allowable concentration, the special reagents and apparatus required, the procedure, and the calculation of results. The substances dealt with in the present series of leaflets are:—chlorine, hydrogen sulphide, aniline, carbon disulphide, ethanol, chromate dust, formaldehyde, diethyl ether, carbon dioxide, acetic acid, styrene, ammonia, hydrogen cyanide, nitrobenzene, lead tetraethyl, nitrous fumes (nitrogen oxides), methanol, acetone, parathion, toluene, and acrylonitrile.

Thomas Bedford

(3434)

BENSON, P. F. & CHISHOLM, J. J., Jr. **A Reliable Qualitative Urine Coproporphyrin Test for Lead Intoxication in Young Children.** *J. Pediatrics.* St. Louis. 1960, June, v. 56, No. 6, 759–67, 3 figs. [16 refs.]

This is a clear, detailed description of the technique of a test for the detection of increased amounts of coproporphyrin in urine which is easy to perform and has proved most useful in the early diagnosis of lead poisoning. The technique is simple and takes only a few minutes but the instructions for its use must be followed carefully. In the test coproporphyrin is extracted from urine by means of ether from which it is in turn extracted by hydrochloric acid. The intensity of the fluorescence in the liquid is then estimated by comparison with standards of known coproporphyrin concentration. In some urines a significant amount of coproporphyrin may be in a non-fluorescent state but can be converted to the fluorescent state by treatment with iodine.

The accuracy of this technique was (1) checked by comparison with results obtained by a quantitative procedure, and (2) evaluated as a screening test in 258 children in whom the diagnosis of lead poisoning was considered.

The test has proved to be most useful. A positive coproporphyrin result (tables are given on arbitrary scales of fluorescence intensity and on a comparison of this intensity as related to whole blood lead concentration) "was present uniformly in patients with whole blood lead concentration greater than 0·10 mg. per 100 Gm., whereas in a number of these patients abdominal and long bone x-rays were negative for evidence of plumbism and the history of pica was denied".

M. E. Delafield

YAMAGUCHI, S. **Clinical and Epidemiological Studies of Tetra-Ethyl-Lead Poisoning in Japan.** *Kyushu J. Med. Sci.* Fukuoka. 1960, Feb., v. 11 No. 1, 37–44, 2 figs. [11 refs.]

Several outbreaks of poisoning in Fukuoka Prefecture, Japan, which were either proved or suspected of being due to tetra-ethyl lead (TEL) have occurred between 1946 and 1957 and are here reported briefly. The total number of cases was 40 of which 20 were in males of whom 6 died and 20 in females with 7 deaths.

The first outbreak occurred in a factory where "an oily substance of unknown nature" was used as a solvent of furniture paint because of a shortage of the proper solvent. 4 of the 7 affected people slept in a heated room in the factory and all were in a "state of violent mania" next morning and 3 died within 24 hours. Absolute proof that the solvent was TEL was not obtained.

The largest outbreak involved 22 persons of whom 7 died, in a community of 120 people. These cases of poisoning occurred sporadically over a period of years. Investigation of information that several oil drums had been buried and hidden since the end of World War II revealed that the water supply which was from wells contained a high concentration of tetra-ethyl lead.

A small outbreak of lead poisoning was found to have resulted from careless handling of tetra-ethyl lead in

cleansing gasoline tanks at an airfield and another outbreak from well water contaminated by tetra-ethyl lead in a drum, bought in the black market, which left unused for some years had corroded and its contents had leaked into the soil. *M. E. Delafield*

IPPEN, H. Die subklinische Bleischädigung. **[Subclinical Lead Poisoning]** *Berufsdermatosen.* Aulendorf. 1960, June, v. 8, No. 3, 139–50, 1 fig. [94 refs.]

This is a long paper in which the author describes and discusses, on the basis of the numerous quoted references, the condition described as sub-clinical lead poisoning. By this term is meant the condition which may be caused by the introduction into the body of small amounts of lead over a period of many years during which no definite manifestation of lead poisoning has occurred. This long exposure to lead may, however, lead to damage of certain organs, of which the liver is the most important. In these cases the toxic hepatosis may develop into a cirrhosis. An external manifestation of this state may be a skin condition such as porphyria cutanea tarda. Such a skin condition results primarily from the hepatosis and is thus only indirectly associated with lead.

In view of this very probable relationship in some instances between a skin condition and a toxic hepatosis it is considered that both the liver condition and the porphyria should be regarded as industrial diseases if prolonged exposure to lead is proved and other causes of liver damage can be excluded. [See also this *Bulletin*, 1960, v. 35, 235.] *M. E. Delafield*

VOIGT, G. E. & LARSSON, L. E. **Distribution of Lead and Mercury in Femur of Acutely Poisoned Rats.** *Acta Path. et Microb. Scandivanica.* 1959, v. 47, No. 3, 256–8, 1 fig.

"In rats treated with lead acetate i.m. and killed 15 minutes to 4 hours later the sulphide silver method showed the presence of metal around and in the Haversian canals. In rats treated with sublimate i.m. streaks of metals were seen in the growth zone of the femur and along the outline of bone trabeculae".

PAYNE, W. W. **Production of Cancers in Mice and Rats by Chromium Compounds.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 530–35, 4 figs. [18 refs.]

This is an extention of previous work [this *Bulletin*, 1960, v. 35, 26] to see whether the 3 chromium compounds administered in a sheep fat vehicle, which produced carcinomata and sarcomata in rats, would do so in another species, and to investigate effects with other vehicles. In 26 male and 26 female mice, thigh muscle implants were made of 10 mgm. calcium chromate or sintered calcium chromate in 20 mgm. sheep fat. In similar groups of mice, subcutaneous injections were made of these 2 compounds or sintered chromium trioxide in 0·2 ml. tricaprylin. In 12 rats, calcium chromate in gelatin capsules was implanted intramuscularly or intrapleurally; the dose was 12·5 mgm., *i.e.*, one half of the dose previously implante in 50 mgm. of fat, because most animals died quick from acute poisoning with 25 mgm. in gelatin.

Spindle cell sarcomata were found at the site of a ministration as follows: in the mice, 11 tumours aft implants between 7 and 13 months, 9 being from th sintered chromate, and only 1 in 18 months after injectio of calcium chromate, this occurring after 12 months; the rats, 5 tumours, between 7 and 12 months, 3 beir among the 6 intrapleural group. No tumours occurre in the other 2 tricaprylin groups or controls receivir sheep fat implants or tricaprylin injections, nor in currer experiments in rats with chromic acetate in capsules.

The evidence that chromium in some form is respo sible for cancer in the lung in chromate workers strengthened by these results. Neither a sheep fat vehic nor a reaction between it and oxidizing chromates essential for the experimental production of the tumours in rats. *M. Patricia Fitzsimons*

SCHÜRMANN, D. Zwei Beryllium-Todesfälle und ihr Lehren. **[Two Beryllium Fatalities and the Implications]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, June, v. 10, No. 6, 139–41.

The difficulty of diagnosis and notification of berylliu poisoning is exemplified in 2 fatal cases described b the author.

The first, a man aged 55, had worked for 8 years a tunnel oven where beryllium carbonate and materia containing beryllium oxide were heated. 4 years lat he developed lung symptons, with X-ray signs of chron bronchitis and increase of interstitial connective tissu A diagnosis of beryllium poisoning was made by th works physician; this was later confirmed by two oth opinions and a 50% disability recognized. Death occurre in 1958, the cause being stated as coronary thrombos No abnormalities characteristic of beryllium disea were found at autopsy, and the apparent granuloma observed during life were ascribed to bronchopneumoni

The second, a man aged 60, had been employed for years in the production of beryllium nitrate from th carbonate; exhaust ventilation and a rubber mask we provided. 2 years later the works physician diagnos bronchial asthma, from which he had suffered for years, made worse by beryllium, but not characteristic berylliosis. His emphysema increased and a year lat X-rays showed increased striation in the right lung, b no stippling or nodulation; compensation for berylliu poisoning was refused. 4 years later the man died, wi severe cyanosis, emphysema and heart failure. At autop the pulmonary lesions were described as absolute typical of chronic berylliosis; no estimation of the ber lium content of the lung was made.

It is concluded that these cases show that while n every person exposed to beryllium develops beryllios refusal of compensation to one who has had defin exposure, even if clinical and X-ray findings are not e tirely characteristic, carries a grave responsibility, and th persons suffering from chronic bronchitis or asthma circulatory disorder should be excluded from worki with beryllium. *E. Browning*

KOIKE, S.; KAWAI, K.; SUGIMOTO, H.; HASEGAWA, H.; SATO, M. **Experimental Studies on Benzene Poisoning. 1. Effect of Benzene on the Blood and Bone Marrow in Albino Rats** [KOIKE, KAWAI & SUGIMOTO]. *Bull. Nat. Inst. Indust. Health.* 1959, No. 2, 1–16, 14 figs. [16 refs.] **2. Effect of Benzene on the Catalase Activity in Blood** [HASEGAWA & SATO]. *Ibid.*, 17–28, 6 figs. [19 refs.]

These studies were carried out on rats acutely poisoned by subcutaneous injections of 1 or 2 ml. benzene per kgm. each day for periods up to 5 weeks.

1. The first paper deals with changes found in rats killed at intervals, *e.g.*, the rapid fall in leucocyte counts, in marrow nucleated counts and in marrow concentrations of deoxyribonucleic acid. With the smaller doses these values tended to improve. This was not so with the larger doses, and some animals showed aplastic marrow. Morphological changes are illustrated. Mitotic disturbances were noted which persisted after regeneration. Erythrocyte counts and marrow concentrations of ribonucleic acid were hardly affected.

2. Reasons are given in the second paper for investigating catalase activity, which was inhibited. Instead of a phenolic substance being responsible, as expected from the metabolic breakdown of benzene, a new non-phenolic substance was extracted from the poisoned rats' blood to which catalase inhibition could be ascribed. It was extracted by acetone, and not by boiling or butanol. The order of inhibitory effect of phenols on catalase prepared from equine liver was catechol>hyroquinone>resorcin>phenol. *M. Patricia Fitzsimons*

CORNISH, H. H. & BLOCK, W. D. **A Study of Carbon Tetrachloride. I. The Effect of Carbon Tetrachloride Inhalation on Rat Serum Enzymes.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 549–54, 3 figs. [11 refs.]

In this study, values for 3 serum enzymes, expressed as percentages of control values, are given for 10-day periods after single 4-hour exposures of rats to 1,500, 1,000 or 250 p.p.m. CCl_4 and also during 10-day exposures for 6 hours daily to 250 or 100 p.p.m. or for 4 hours daily to 100 or 50 p.p.m. Where changes were found, they were increases in glutamic-oxalacetic transaminase (GOT) and xanthine oxidase, and decreases in esterase. The extent of change bore a direct relationship to the degree of exposure. The variations were generally more marked in the female rats. The greatest changes were in GOT values. Marked changes in all 3 enzymes were found at 1,000 or 1,500 p.p.m. but none below 250 in other single exposures. With the repeated 6-hour exposures, gradual changes were found, but with the shorter and lower concentrations only the esterase was affected.

Inanition due to CCl_4 was not responsible for the results, because the effects of 5 days' starvation on other rats were found to be negative except for a transient slight increase of GOT.

In vitro studies, in which 0·2 ml. CCl_4 was added to 2 ml. rat serum, showed enzyme activity in all 3 cases to be similar to each activity of untreated serum. The changes found in the experimental animals therefore represent changes in the amounts of enzymes in the serum. The increases in GOT and xanthine may be due to release of enzymes from damaged tissues, especially from the liver, and the decrease in esterase to a decreased ability of the liver to synthesize the esterase enzymes at the normal rate. *M. Patricia Fitzsimons*

NORO, L. & PETTERSSON, T. Metylkloridförgiftning. [**Methylchloride Poisoning**] *Nordisk Med.* 1960, July 14, v. 64, No. 28, 881–4, 2 figs. [12 refs.] English summary.

The English summary appended to the paper is as follows:—

"After a review of earlier observations on methylchloride poisoning the writers report on five cases of poisoning caused by a leaking refrigerator in an apartment. One of the cases ended in death.

"Symptoms of poisoning were nausea, stomach pains, halitosis, hiccup, diplopia, disturbance of vision, clonic cramp, and mental confusion. These were all in accordance with symptoms previously mentioned in the literature. Other observations were slight leukocytosis in two cases, and lowering of the S–T segment in the electrocardiogram. Headache, leg weakness, and tendency to collapse were observed as late symptoms.

"The health authorities should pay close attention to the use of methylchloride in refrigerators. Preferably its use should be prohibited altogether in refrigerators installed in apartments."

HAAS, P. A. Industriehygienische Untersuchungen über das Trichloraethylen in der metallverarbeitenden Industrie. [**Industrial-hygienic Investigations of Trichloroethylene in the Metal Industry**] [Thesis.] 152 pp., 23 figs. [268 refs.] Prom. Nr. 2979. 1960. Zurich: Ozalid AG.

This monograph on trichloroethylene, with particular reference to the metal industry in Switzerland, gives a comprehensive account of its production, chemical properties, general uses, metabolism, estimation of metabolites and of air concentrations, relation between clinical findings and chemical analyses, and prevention of injury to the health of workers. An enumeration of the many products with trade names which do not suggest their content of trichloroethylene includes a warning that the commonly used abbreviation "Tri" is applied also to substances such as tricresyl phosphate and trinitrotoluol.

On the controversial question of the correlation of its two chief metabolites, trichloroacetic acid and trichloroethanol, with the degree of exposure, HAAS concludes from his own observations on workmen in the machine industry that a high concentration of trichloroacetic acid in the urine is not necessarily the result of an average daily exposure but may be due to an occasional, rare

high concentration, and that the extreme individual variations of urinary trichloroacetic acid militate against its value as a measure of exposure. Estimations, carried out by a modified Fujiwara reaction, gave values between 8 and 444 mgm. per litre. A definite correlation between the incidence of neurological disturbance and increasing air concentrations of trichloroethylene, and between excretion of trichloroacetic acid and duration of exposure have led the author to recommend a lowering of the widely accepted MAC of 200 p.p.m. to 40 p.p.m.

While a statistical account of the incidence of neurological, vegetative and psycho-organic changes is of interest in confirming the opinion of other authorities that these effects of chronic exposure to relatively low concentrations do occur, it is somewhat disappointing from the toxicological point of view that these are not more fully described; they are related only briefly to the results of chemical analysis.

In the measures of prevention, special emphasis is laid on instruction of workers in careful handling, and on thermostatic control of the temperature of the solvent.

Ethel Browning

OLMSTEAD, E. V. **Pathological Changes in Ethylene Dibromide Poisoning.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 525–9, 4 figs.

This case report has illustrations showing the massive central lobular necrosis of the liver and focal necrosis in the proximal tubules of the kidney, the result of ingesting 9 soil-fumigant capsules, each containing 0·5 ml. ethylene dibromide. The substance, 1:2 dibromoethane, $CH_2Br\text{-}CH_2Br$, is available in pellet form for control of ground pests, and is also used in "leaded" petrols and as a chemical intermediate.

The patient, a woman aged 43, had taken alcohol in excess for mental depression for several years, and had recently been investigated twice for upper abdominal pain, with negative results. Vomiting started almost immediately after the capsules were swallowed, and this continued with pain, tachypnoea, agitation and later diarrhoea and oliguria until admission to hospital 48 hours later. She was then anuric. Supportive therapy was given, but she died in 4 hours. The only other signs were slight icterus, pyrexia, tachycardia, hypotension and a conducted systolic murmur at the apex. The results of several blood and serum investigations are given and a full description of the necropsy findings. Apart from the liver and kidney changes already mentioned, there were no liver changes attributable to alcohol and only minimal inflammatory reaction, and there was no evidence of haemoglobinuric nephrosis. The gastro-intestinal tract showed reddening and inflammation, but no ulceration. The anuria was ascribed to fluid loss from the gastro-intestinal tract coupled with profound shock from the extensive hepatic necrosis. The effect of the chemical may have been enhanced by the excessive alcohol intake, though the liver and kidney changes were similar to those found in oral toxicity studies, with the new observation on the part of the kidney tubules involved.

M. Patricia Fitzsimons

KRÜGER, P. D., ZORN, O. & PORTHEINE, F. Problem akuter und chronischer Kohlenoxyd-Vergiftungen **[Problems of Acute and Chronic Carbon Monoxid Poisoning]** *Arch. f. Gewerbepath. u. Gewerbehyg* 1960, v. 18, No. 1, 1–21, 2 figs. [Numerous refs.]

The increasing danger to man of the ubiquitous carbo monoxide — a poison of civilization — the frequen transitory effects of exposure to the gas, the difficultie of certain diagnosis of slight acute poisoning and th conflict of opinion about chronic carbon monoxid poisoning would appear to make it necessary to revie the toxicological and clinical problems in the light of th literature and up-to-date experiences.

There is here a lengthy description and discussion o the physical and biological characteristics of carbo monoxide, of physiological facts about its combinatio with haemoglobin, concentration of CO-haemoglobin i workers in different industries, errors in methods o estimation of CO and the clinical findings in surveys o workers and workplaces.

The main conclusion is that "chronic CO-poisoning" in the real sense does not exist, but that in instances i which the workers in certain industries are from time t time exposed to moderately high concentrations o carbon monoxide, they may complain of subjectiv symptoms of fleeting nature (headache, giddiness an feelings of weakness). If these symptoms occu repeatedly then the condition is rightly to be called recurrent slight acute carbon monoxide poisonin (*rezidivierende, leichte (akute) CO-Vergiftung*).

M. E. Delafield

PETRY, H. Gegenwärtiger Stand unseres Wissens übe die chronische Kohlenoxydvergiftung. **[Presen State of Knowledge of Chronic Carbon Monoxid Poisoning]** *Arch. f. Gewerbepath. u. Gewerbehyg* 1960, v. 18, No. 1, 22–36. [46 refs.]

In this paper the author gives an interesting discussio based on his own observations and other references i the literature, which have a bearing on the conflictin opinions expressed in the last few decades, on the que tion of whether or not there exists a true condition c chronic carbon monoxide poisoning.

There is a critical examination of these from which is concluded that the number of recorded cases co sidered to be chronic poisoning is not large, at any ra in the industrial sphere. It is maintained, however, that a people in some occupations such as technicians, chemis and drivers of vehicles may be exposed to the inhalatio of carbon monoxide from time to time, and suffer i health in various ways, better knowledge of the subje on the part of medical practitioners would prevent mi diagnosis. Better prophylactic measures are also neede Such cases of illness resulting from exposure to carbo monoxide from time to time are considered by th author to be reasonably called "chronic carbo monoxide poisoning" and he regards as hair-splitting th attempts of some workers to replace this designation b "recurrent slight carbon monoxide poisoning" (*rez divierende leichte Kohlenoxydvergiftung*). [See KRÜG *et al.*, above.]

M. E. Delafield

Balchum, O. J., Dybicki, J. & Meneely, G. R. **The Dynamics of Sulfur Dioxide Inhalation, Absorption, Distribution, and Retention.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 564–9. [13 refs.]

This article describes experiments in dogs with SO_2 tagged with $^{35}SO_2$ to determine how much was absorbed *in vivo* by an isolated length of trachea, how long it remained in tissues after intratracheal administration and whether tissue distributions after intra-arterial injection of $Na^{35}SO_2$ or after inhalation of the gas-air mixture differed. Previous experiments [in the Press] had shown that when it was inhaled through a tracheostomy it was rapidly absorbed and distributed to all tissues, including the brain, with a relatively high retention by the trachea, lungs, hilar lymph nodes, liver, spleen and kidney, and that when it was inhaled through nose and mouth, in concentrations of 1 to 141 p.p.m., a large proportion remained in the upper airways, a greatly reduced quantity reaching the trachea and lungs, and then other viscera.

Enough was absorbed when the trachea alone was perfused to decrease compliance and to increase pulmonary resistance. Other tables show an appreciable amount in liver, spleen and kidneys and greater concentrations in lungs, oesophagus, hilar nodes and trachea. Other dogs inhaled through an intratracheal tube for 40 minutes and at least 90% of the $^{35}SO_2$ per unit of gas-air mixture was retained. Tissue concentrations are shown in dogs killed 2 and 7 days later, and even in the latter appreciable concentrations were present in respiratory tract tisues when compared with concentrations found in the previous experiments in dogs which were killed 40 minutes after inhaling similar quantities through a tracheostomy. Therefore ^{35}S is retained in the lungs and trachea for as long as 7 days. Concentrations in trachea and lung were much lower after intra-arterial $Na^{35}SO_2$ than after inhalation of $^{35}SO_2$ in amounts which had one-tenth of the activity of the injected solution; measurements were made after the same intervals in both experiments, and concentrations in other tissues were similar in both. *M. Patricia Fitzsimons*

Kropst, A. Über die Vergiftung mit nitrosen Gasen. [**Poisoning by Nitrous Gases**] *Wien. med. Woch.* 1960, July 9, v. 110, No. 27, 591–6, 6 figs. [22 refs.]

Poisoning by oxides of nitrogen—NO_2, N_2O_4, NO and N_2O_3—and also by the formation of nitrous and nitric acids may be a risk to workers in many industries. Numerous fatalities in industrial workers have been reported in the literature. Opinions on the toxicology of these substances are not in entire accord. Some observers consider that the chief effect is on the pulmonary system through the local formation of nitric acid which causes pulmonary oedema, but others take the view that a general, systemic poisoning is brought about by the formation of nitrite.

This paper contains a detailed report of a man aged 35 years who was engaged at a steel works in cleaning out a drainage pit which contained some steel plate, with nitric acid and additions of salt and sulphuric acid. After the end of his shift he was taken ill with giddiness and some difficulty of breathing and cough. His condition deteriorated rapidly and he died after 3 days from pulmonary oedema. There is a full account of the post-mortem findings, including photographs of the microscopic appearances of the lung and the results of spectrophotometric examination of blood taken from the heart.

There is a full discussion. The chief toxic changes were found to be those of local pulmonary irritation caused by the formation of nitric acid. Evidence of systemic poisoning, however, was found in the general dilatation of blood vessels, blood stasis and fatty changes in the liver which resulted from the formation of methaemoglobin, nitrogen oxide haemoglobin and nitrite demonstrated by spectrophotometry.

M. E. Delafield

Stumpe, A. R. **Toxicity of Diborane in High Concentrations.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 519–24, 6 figs. [11 refs.]

Investigations with high concentrations of this toxic gas, necessary because of the possibility of accidental cabin contamination during flight, confirm that aircraft and rockets fuelled with the boranes should be designed to provide against this. Diborane can be detected by odour at 2·8–3·6 p.p.m., but the threshold limit value is 0·1 p.p.m. It is rapidly hydrolysed with release of heat and formation of boric acid, but its toxic mechanism is not yet clear.

Golden hamsters were exposed to 11 concentrations from 50 to 1,000 p.p.m. of diborane which had been diluted with nitrogen, to diminish the explosive risk, and compressed air. Each experiment continued until all in each group were dead. Controls were exposed to a 10% nitrogen-air mixture for 2 hours and then killed. They showed only inactivity and pulmonary changes from strangulation.

The test animals quickly became inactive. Then restlessness and increased activity were accompanied by falling. The upright position could be regained until hyperpnoea developed. Terminally, respiration decreased in depth and rate with prolonged periods of apnoea. From concentrations up to 400 p.p.m., the lungs were bright red, and above this dark reddish brown. Vascular congestion, oedema, epithelial sloughing, alveolar blood cells and areas of atelectasis and emphysema were present in all, more marked above 400 p.p.m. The liver showed no microscopic changes, the kidneys, especially the glomeruli, some congestion. Even with diffuse pulmonary changes, there remained a minimum time for irreversible changes to develop, irrespective of raising the concentrations. This interval of approximately 25–35 minutes persisted for concentrations above 600 p.p.m.

A time-concentration curve shows from 50 to 600 p.p.m. progressive shortening of the mean exposure time for death, from 497 to 33 minutes, and also narrowing of the range around each mean. Above 600 p.p.m. there were no further reductions in minimum, maximum or mean fatal exposure times. *M. Patricia Fitzsimons*

ROCHE, L., RAVAULT, P. P., VIGNON, G., LEJEUNE, E., MAITREPIERRE, J. & LAMBERT, R. Deux nouvelles observations d'ostéopétrose fluorée. [**Two Cases of Fluoride Osteosclerosis**] *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 356–7.

The 2 cases of marked bony changes due to fluoride reported here were in patients who did not appear to be greatly affected by the condition which is described as clinically latent.

The first patient, a man of 55 years, had been working for 20 years as a supervisor in an electrolytic aluminium works. For about a year he had had pains in the back, neck and legs but chiefly after prolonged effort. Admitted to hospital for renal colic, he was examined by X-ray when the condition of the bones was discovered. This condition of osteosclerosis which is fully described was most marked in the spine, pelvis, arms and legs. His teeth showed the classical picture of dental fluorosis. Chemical analysis of the teeth showed a fluoride content of 53·3 mgm. per 100 gm.

The second patient aged 58 years had worked from the age of 25 to 35 years in the phosphate mines of Tunisia. For the last 20 years he had had pains in the elbows, knees and ankles while at work or when walking. X-ray revealed generalized osteosclerotic changes. His teeth also showed fluoride changes and their fluoride content was 156 mgm. per 100 gm. [See also CHAMPEIX, below.]

M. E. Delafield

CHAMPEIX, J. Observations récentes d'ostéopétrose fluorée professionnelle. [**Some Recent Observation on Industrial Fluoride Osteosclerosis**] *Arch. Malad. Professionnelles.* Paris. 1960, June, v. 21, No. 6, 357–61, 2 figs.

The introduction to a report on 2 cases of osteosclerosis due to fluoride gives a list of the manufactures of hydrofluoric acid, metallic fluorides, fluosilicates and fluoborates in which workers are exposed to risk. 4 other similar cases were reported previously (*Ann. Méd. Légale et de Criminol.* 1954, v. 34, 253).

The present report concerns 2 workers in these manufactures—a man aged 59 engaged in this work for 38 years and the other aged 61 years exposed to risk for 23 years. Both men appear to have continued at work without definite symptoms and only slight stiffness. There is a description of the results of laboratory and clinical examinations.

The general X-ray characters of fluoride osteosclerosis are described in detail. There is an increase in bone density, particularly in the spine, but other bones are also involved. Osteophytes and calcification of ligaments and muscle attachments are frequently seen. It is also stated that there are 2 main types of fluoride osteosclerosis which may be differentiated by X-ray examination.

M. E. Delafield

WILSON, R. H. & MCCORMICK, W. E. **Plastics. The Toxicology of Synthetic Resins.** *Arch. Indust. Health.* Chicago. 1960, June, v. 21, No. 6, 536–48. [114 refs.]

This third revision of an earlier paper [this *Bulletin*, 1955, v. 30, 329] classifies synthetic resins into 15 groups, *viz.*, acrylic resins, alkyd resins, amino (urea and mela mine) resins, cellulose plastic materials, coumarone-inden resins, epoxies, fluorocarbons, nylon, phenolic resin polyethylene, polyester resins, silicones, polystyrene, viny resins and polyurethanes.

Though polymerized resins in themselves are usuall not toxic, a risk may arise from plasticizers, lubricant stabilizers, colours and fillers used with them to form the finished plastic, and there may be risks in the manu facture of the monomers of these resins. Plastics ar widely used in surgery and in food containers; and when animal experiments have resulted in tumour formation this is stated [though in the appropriate summary it often ignored, presumably because of some uncertainty

The uses of compounds in each group show similaritie and contrasts: the toxic properties of the group, if known can be guarded against in the diverse manufacturing pro cesses and uses inherent in such a multiplicity of article The risk in use is generally none or remote.

Apart from dermatitis or tissue reaction which ar noted in some summaries, points noted in summaries ar as follows. Methyl methacrylate vapours have som systemic effect. Amino resins can in certain combination pyrolyse to HCN and CO; the aminoplasts may be toxi Internal use of cellulose plastics may be hazardous; i manufacture of cellulose acetate there is a risk fro acetic acid. Fluorocarbons may decompose at hig temperatures into irritant, toxic products. In the manu facture of polystyrene, some hazards are encountere especially from ethylbenzene, and several hazards occu during manufacture of polyurethanes because of the u of isocyanates.

M. Patricia Fitzsimons

WASSERMANN, M., ILIESCU, S., MANDRIC, G. HORVATH, P. **Toxic Hazards during DDT- an BHC-Spraying of Forests against** *Lymantri monacha. Arch. Indust. Health.* Chicago. 196 June, v. 21, No. 6, 503–8, 4 figs.

This report from Rumania describes the problems a 30-day operation of combined aircraft and groun spraying in difficult mountainous country. At first the were frequent accidents, partly caused by the hors falling, possibly because they were not protected by re pirators. Men and horses were injured and becam contaminated by the insecticides. The men, therefo who had been provided with protective clothing, work only in teams. Mixtures of the gamma isomer of benzen hexachloride and DDT were sprayed as dusts, solution and aerosols by various methods, and were effective ridding the coniferous forests of a heavy infection the destructive indigenous caterpillar. Cold winters ha killed many of its enemies and hot rainy summers ha favoured it. Abrupt slopes and deep valleys were spray by ground crews. Where paths had to be cut, each m used a Swingfog spray, weighing 20 kgm. Horses carri the bulk solutions. A tractor carried the S–811 apparat which produced a 200-metre fog column. Each S–6 apparatus, which could be pulled by horses, produced 50-metre dust column. The airplanes for the mounta tops and wide valleys had to be loaded with 800 kgm. in minutes.

Tables show breathing zone concentrations of ea

insecticide and the calculated 8-hour respiratory exposures to each and to the mixtures, and also the skin exposure from S–612. Total respiratory exposures ranged from 0·91 to 3·36 mgm. per kgm. per 8 hours, and in airplane work from 19 to 26; dermal exposure was 32 mgm. per kgm. per 8 hours. Erythema after falls, dermatitis from S–612 work and conjunctival, respiratory and gastro-intestinal irritation, mainly among Swingfog and airport workers, disappeared in the majority in 3–4 weeks after spraying ceased. Airport workers' urine contained 2–4 mgm. BHC per litre for a short time.

Cattle and beehives had been removed. Wild animals and birds left during the spraying, but returned afterwards. Pollution of air, soil and water was insignificant. Rivers became clear of BHC after rain, and fish were unaffected. The entomological problem is, however, complex and is being investigated. *M. Patricia Fitzsimons*

Bauer, H. Bestimmung der Cholenesterasen im Blut und neurologische Überwachung bei beruflicher Gefährdung durch Organophosphate. [**Determination of Cholinesterase in the Blood and Neurological Supervision of Occupational Risks from Organic Phosphates**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 1, 91–106, 4 figs. & 4 diagrams. [Numerous refs.]

In this paper there is a detailed description of a modification of the method of Michel (*J. Lab. Clin. Med.*, 1949, v. 34, 1564) for the determination of red blood cell and plasma cholinesterase activity which is stated to be simple to manage and suitable for routine use in the clinical laboratory. The results obtained with it are discussed at some length.

This method of blood examination was used together with neurological control examination in workers engaged in the manufacture of the organic phosphate insecticide Diazinon. The main finding was that the cholinesterase activity in the blood diminishes markedly before any clinical signs of an intoxication are manifest. There is discussion of the importance of the acetylcholine-cholinesterase system, of the effect of organic phosphate on this and hence on the transmission of nerve impulses and on the central nervous system *M. E. Delafield*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

Semple, A. B. **Some Recent Problems of Imported Food.** *Med. Officer.* 1960, Aug. 5, v. 104, No. 6, 101–5.

Major food problems during the last 5 years have been concerned with egg products from China and Australia, frozen prawns from Japan and desiccated coconut from Ceylon.

The first shipment of Chinese frozen whole egg reached Liverpool in January, 1955, and in one year 440 tons had been landed. The isolation of many salmonellae including *Salmonella typhi-murium* and *Salm. paratyphi B* raised many difficulties of sampling and of disposal.

There were three major practical defects. (1) There was lack of intercommunication between sea ports so that each port was acting independently; in some instances tins of Chinese egg condemned in one port were transferred to another, less particular about accepting contaminated goods. Direct and rapid exchange of information between the 10 major sampling ports with collateral information for the Ministry would have eased the situation. Egg products from Australia produced similar problems but the Australian High Commission assisted with matters of coding. (2) Little information was available on the pathogenicity of the various salmonella serotypes. (3) Results of examination were not reliable in their ability to detect contamination by normal methods of sampling, because the distribution of bacteria throughout a pack was not homogeneous; examples are given.

Results showed that the institution of bacteriological standards for imported cooked frozen prawns from Japan had produced a great improvement in conditions at packing and cooking stations.

It was agreed that the general colony and staphylococcal counts should be limited, but the numbers to be allowed were still under discussion. The exclusion of salmonellae in 50 gm. and a standard for faecal coliform organisms were also desirable. No bacteria had been found in the gut contents of the cooked prawns and thus contamination was human and environmental in origin and could be avoided by suitable measures.

Chinese shrimps presented similar problems, and it is stressed that technical support is needed for assessing the bacteriological acceptability of a product.

The current problem is concerned with the annual importation of 6,000 tons of Ceylonese coconut, a variable proportion of which is contaminated with a wide range of salmonellae including *paratyphi B, typhi-murium,* Thompson, Bareilly, Hvittingfoss, Waycross, Newport, Münster, Poona, Angoda, Perth and Senftenberg. Consignments are detained if a 5% followed by a 10%

sampling reveal the presence of *Salm. paratyphi B* and *typhi–murium* or Thompson. [The isolation of other serotypes is apparently disregarded although some of them commonly cause outbreaks and sporadic cases.] In Liverpool 1,636 samples had been taken from 332 consignments this year, and 1,574 packages had been rejected. The trade had organized investigation of the mills in Ceylon and there were recommendations designed to improve the hygiene of the process; a coding scheme for mill identification had been proposed.

Methods of decontamination by heat (steam and dry), ultra-violet light, radiation, fumigation by ethylene oxide and ultrasonic impulses are mentioned.

It is emphasized that there should be direct communication between the medical officers of health of the 10 major food-importing seaports and a form is suggested for exchange of information on contamination of food coming into these ports. Both the Ministries of Health and Food would be notified at the same time as the other ports.

Where a continuous import such as egg products or desiccated coconut is concerned, meetings should be arranged to ensure that action is uniform and a definite standard agreed; medical epidemiologists are considered necessary adjuncts to such meetings.

Agreement should be reached on the application of standards to ensure that concerted requests are put forward to the importers. All decisions should be strengthened by technical information. *Betty C. Hobbs*

TEN CATE, L. De microbiologie der "geschwitzte" snijworst. [**The Microbiology of Tempered Dry Sausage**] *Tijdschr. v. Diergeneesk.* 1960, June 15, v. 85, No. 12, 743–51. [21 refs.] English summary.

A survey was conducted of the bacterial flora present during the manufacture of tempered dry sausage. The microbiology was investigated in the raw sausage-dough, 2 days after the start of the cold smoking (tempering) process, after the end of smoking, and after 1, 2, 3 and 4 weeks' drying.

25 gm. of sausage were homogenized with 225 cc. of sterile chilled 4% brine and dilutions of 1 in 1,000, 1 in 1,000,000 and 1 in 10,000,000 were plated on ordinary agar and various special media. In the raw sausage there was a bacterial count of 200 million per gm., which consisted mostly of common flora, and which completely died off in the first day of the tempering process and was followed by a growth of lactobacilli. These attained a count of 100 million during the smoking process, and persisted for 2 weeks of the drying process, after which they declined. Group D streptococci were also present and rose to a maximum count of 200 million on the first day of smoking and died out after the first week of drying.

The disappearance of the two different populations of the common flora and the streptococci during the processing of the sausage can be ascribed to the productio of lactic acid by the lactobacilli from the sugar adde during the process of manufacture. Putrefaction is thu prevented and the production of lactic acid is therefor an essential part of the process of production.

Anne Tothill

WORLD HEALTH ORGANIZATION. TECHNICAL REPOR SER. NO. 197. **Joint FAO/WHO Expert Com mittee on Milk Hygiene. Second Report** Geneva, 13–18 July 1959. 55 pp. [Refs. in foot notes.] 1960. Geneva: Palais des Nations. [Sale agent for U.K., H.M. Stationery Office.] [3s. 6d. $0.60; Sw.fr. 2.–.] Issued also as *FAO Agricultur Studies*, No. 52.]

The first report of the joint Food and Agricultur Organization (FAO) and World Health Organizatio Expert Committee on Milk Hygiene was prepared i 1956 [see this *Bulletin*, 1958, v. 33, 154]. This secon report is presented by that committee which met in Jul 1959, "to review advances concerning the productio and distribution" of fluid and dried milk the hygiene c which was principally considered in the first report. Th Committee in 1959 was also requested "to cover hygien problems concerning milk products, and also to giv special attention to milk hygiene problems in warm weather countries and especially in those countries sti at a low stage of technical development".

This second report is clearly written and well pre sented. It is concerned only with "certain importan new findings and developments" since 1956.

Section 2 on hygiene of liquid-milk covers:— (a diseases transmitted by milk—staphylococcal enterotoxi poisoning, staphylococcosis, streptococcal infections an tick-borne encephalitis, (b) antibiotics in milk, (c) insect cides in milk, (d) radionuclides in milk, (e) bulk dispensin of pasteurized milk and cream, (f) bacteriological tes and (g) pasteurization and sterilization in relation t hygienic quality.

Section 3 covers diseases transmitted through mil products, storage and handling of dried milk, chees butter, ice-cream, cream, fermented milk and flavoure milk; and hygiene control in the production of evaporate and condensed milk.

Section 4 is concerned with the adequacy and qualit of the water supply and with the disposal of milk waste

Section 5 on special problems of milk hygiene in warm countries contains sub-sections on (1) hydrogen-peroxid as a preservative for milk, (2) buffalo milk and (3) shee and goat milk.

There are 2 annexes to the report entitled (1) code c principles concerning milk and milk products and (2 definitions and notes on some milk products.

References to the published reports of various agencie and scientific papers on which this report is largely base are given in footnotes. *M. E. Delafield*

FOOD POISONING

GEMMILL, J. S. & MANDERSON, W. G. **Neurotoxic Mussel Poisoning.** *Lancet.* 1960, Aug. 6, 307–9. [10 refs.]

3 patients were involved in the first outbreak of neurotoxic mussel poisoning recorded in Scotland since 1827. Symptons, tingling and numbness of hands and mouth, weakness of the legs and ataxia, nausea without vomiting, salivation, dysphagia, incoordination, and vertigo, but with mental clarity, began within 30 minutes to 2 hours after eating cooked mussels which had been knocked off logs from a storage dock 2 days previously. The patients revived after 1–3 days. A sample of mussels from the same source showed 15 *Escherichia coli* per ml. of tissue; *Clostridium botulinum* was not isolated.

Water samples were taken from the dock and found to contain *Euglena* and *Peridians* including [probably] *Gonyaulax orientalis* and *G. tamarensis.* It has been claimed in the United States that *G. catanella,* which was not found in this outbreak, elaborates an alkaloid which can be extracted as the hydrochloride; this dinoflagellate inhabits ocean plankton eaten by the mussels. It is not indigenous to the plankton of Europe and cannot be clearly incriminated in European outbreaks [this *Bulletin,* 1958, v. 33, 155]. The danger was eliminated by clearing all logs of shellfish. *Betty C. Hobbs*

CUTTIAUX, R. & VAN AGT, J. Sur une épidémie de toxi-infections alimentaires provoqueés par des crèmes glacées. Utilité épidémiologique d'un examen bactériologique détaillé. Insuffisance des mesures prises pour les éviter. [**An Outbreak of Food Poisoning from Ice Cream. Epidemiological Importance of Full Bacteriological Examination. Inadequacy of Precautions Taken**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1960, Apr.–May, v. 8, No. 3, 211–16.

Between 9 and 11 July, 1958, 200–400 cases of gastro-enteritis, mostly among children 5–12 years of age, occurred in a built-up coastal area in the North of France. Symptoms of diarrhoea and vomiting commenced 8–12 hours after eating ice-cream contaminated with *Salmonella typhi-murium* and made by an itinerant vendor. The patients were treated with chloramphenicol. *Salm. typhi-murium* phage type Ia was isolated from the faeces of 12 patients, the vendor and his wife, 2 of 3 daughters and from the ice-cream; the various strains differed in a sensitivity to aureomycin. The man had eaten mussels from a barrow the day before the outbreak and had suffered gastro-enteritis; his strain was resistant to the antibiotic; his wife was carrying a sensitive strain. One daughter had been ill the previous year with a paratyphoid-like illness and had suffered gastro-enteritis 3 months before the outbreak; it is thought that she may have infected her mother. The second daughter was ill after eating contaminated ice-cream. An employee and the youngest daughter were free from infection and ill-ness. Strains both sensitive and resistant to various anti-biotics were found in batches of ice-cream and also in the stools of patients.

The ice-cream was prepared in a room adjoining the home of the family and the ingredients included milk, egg yolk, sugar and a stabilizer. The milk was obtained raw from a local farm, it was heated and left to cool overnight at atmospheric temperature, 20°–22°C. It was thought to have been contaminated by the man and his wife while removing the skin, and there was opportunity for the organism to grow in the 6–7 hours' storage before admixture with the other ingredients. The mix was frozen within 20 minutes.

The authors emphasize the danger from the handling of perishable or preserved foodstuffs by carriers of intestinal pathogens, and state that the number of outbreaks of salmonellosis and staphylococcal intoxication from ice-cream is increasing in France. Neglect of the Ministry of Agriculture decree of 1949, that milk used in the preparation of ice-cream must be cooled to a temperature not greater than 6°C. if it is not used within 2 hours of pasteurization, caused the present outbreak.

The Conseil Supérieur d'Hygiène Publique de France had made recommendations relating to the preparation of ice-cream by small manaufacturers, but these recommendations were not observed by all administrative authorities.

It is stressed that the bacteriological control of ice-cream is indispensable. *Betty C. Hobbs*

HODGE, B. E. **Control of Staphylococcal Food Poisoning.** *Pub. Health Rep.* Wash. 1960, Apr., v. 75, No. 4, 355–61. [17 refs.]

Staphylococcal enterotoxin food poisoning, the most prevalent cause of food poisoning in the U.S.A., showed no decrease in incidence and 95 outbreaks occurring in 1955 and 1956 were surveyed. In 75 staphylococcal outbreaks, 53 staphylococci were classified as coagulase-positive, 5 as coagulase-negative, 45 as *Staphylococcus aureus,* 1 as *Staph. albus* and 28 as haemolytic. In 77 outbreaks 79% showed incubation periods of 1–4 hours, 14% of 5–8 hours, and 6·5% more than 8 hours.

In 94 outbreaks the vehicle was reported to be cooked food containing a large proportion of protein; in 63 outbreaks (67%) vehicles were food mixtures such as tuna salad, turkey salad, creamed chicken, potato salad, meat loaf, chicken pie, egg salad, and cream-filled pastries, all of which may be handled after cooking. Raw and freshly cooked meats and vegetables unmixed with high-protein foods were not reported.

Visible infections of food handlers were reported in 9 outbreaks, insanitary practices in 13, and in 21 outbreaks both infections of food handlers and uncleanliness of environment were reported. In 50 outbreaks neither infections of food handlers nor uncleanliness was observed. It was assumed that the frequent occurrence of pathogenic staphylococci among healthy persons ensured widespread contamination of food regardless of care in handling.

Left-over food was reported as the vehicle in 81 outbreaks, in only 5 was the food cooked on the day of consumption, and unrefrigerated food was reported in

74 of 83 outbreaks. The length of time the food was left unrefrigerated varied from 4 to 8 hours or was unknown.

It was concluded that the occurrence of staphylococcal enterotoxin food poisoning was determined by leaving cooked protein food warm or at room temperature for 4 hours or longer. Faults included placing food in warm ovens, keeping food on a steam table for many hours after the steam has been turned off, mixing hot and cold foods without subsequent heating, warming left-over food without thorough heating throughout, and judging th temperature of the food by that of the waterbath.

Recommendations for the control of staphylococc food poisoning should aim to prevent the production enterotoxin.

The following standards were arbitrarily chosen protect cooked protein foods: 40°F. as the maximu temperature for keeping cold, 140°F. as the minimu temperature for keeping hot, and 3 hours as the maximu length of time for storage between 40° and 140°F.

Betty C. Hobbs

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

PRATT, Reta & CARMICHAEL, J. W. **Mold Flora of Human Scalp Hair.** *Mycopathologia.* The Hague. 1960, July 30, v. 13, No. 2, 133–4.

" Samples of human scalp hair were collected in barber shops. Cultures from 97 samples yielded a variety of common molds, but no dermatophytes or other keratinolytic fungi ".

LA TOUCHE, C. J. **Mouse Favus due to *Trichophyton quinckeanum* (Zopf) MacLeod & Muende: a Reappraisal in the Light of Recent Investigations. I & II.** *Mycopathologia.* The Hague. 1959, Nov. 30, v. 11, No. 4, 257–76, 6 figs. on 3 pls. [36 refs.] **III.** *Ibid.*, 277–86, 9 figs. on 5 pls.

The review of the literature which opens Part I supplements the recent comprehensive survey by F. BLANK (*Canadian J. Microbiol.*, 1957, v. 3, 885) of *Trichophyton quinckeanum.* This is followed by a tabulation of the chief features of 22 human cases seen at Leeds during 1951–58 and details of 2 cases in cats. Scalp lesions were noted in only 3 of the human cases, lesions in the others being on glabrous skin, and in only 2 were scutula observed. Scutula were present in both the feline cases; in one there were large favic crusts.

Part II records the successful experimental infection of kittens, mice, and guineapigs. In all three hosts scutula were a primary response but in guineapigs they were masked by excessive inflammatory reaction. Hair became infected and showed a green fluorescence under Wood's light.

Part III deals with the histopathology of *T. quinckeanum* infections. In material from a spontaneously infected kitten the pathogen was seen to have invaded the stratum corneum and also the hair shafts and the inner follicle sheaths, and to have produced arthrospores both in and on the hair shaft. " The main inflammatory response the host . . . showed itself in the massive infiltration the dermal and epidermal tissues in the affected areas serous exudate and polymorphonuclear leucocytes; oth features being the undermining of the scutulum by poc of pus, the formation of discrete peri-follicular micr abscesses in the dermis, the engorgement of capillari and oedema and lastly the parakeratosis." Materi from guineapigs and mice showed similar features.

G. C. Ainsworth

BENSEL, A. **Treatment of Tinea Capitis in Childr with Griseofulvin.** *Amer. J. Dis. Children.* 19 July, v. 100, No. 1, 131–2.

RAUBITSCHEK, F., BIRNBAUM, D. & RAKOVER, J. **Hist plasmin Sensitivity in Israel.** *J. Lab. & Cl Med.* 1960, July, v. 56, No. 1, 133–5. [15 refs.]

" No histoplasmin skin sensitivity was found amo 319 patients examined in various departments of t Hadassah University Hospital. No cross sensitiv between histoplasmin or tuberculin or trichophytin w found."

LOEWENTHAL, L. J. A. **Sporotrichosis treated wi Griseofulvin.** *Med. Proc.* Johannesburg. 19 Dec. 26, v. 5, No. 26, 563–4.

Although the therapeutic efficacy of orally administer griseofulvin is now widely acclaimed its use as a therap tic agent has been restricted in the main to skin disea caused by dermatophytes. Occasionally, claims are ma for its successful application in the case of other diseas for example, in mycetoma due to *Nocardia brasilien* and in sporotrichosis. Acting on such information, t author treated 2 cases of sporotrichosis with this drug

The first patient was a white male aged 48 years who presented with a lesion on the left hand and "bean-sized nodules" along the line of the lymphatic drainage on the forearm. *Sporotrichum schenckii* was grown in culture from the hand lesion.

Oral treatment with griseofulvin in the dosage of 250 mgm. 4 times daily, resulted in clinical improvement 2 weeks later. After a further 2 weeks' treatment "the hand and the arm appeared completely normal".

The second patient was a white male aged 44 years who presented with a lacerated lesion on the right wrist where a splinter from a pit prop had entered; the pus yielded *S. schenckii*. Orally administered griseofulvin given in the same dosage as in the previously-mentioned case resulted in complete resolution after about 4 weeks' treatment. *C. J. La Touche*

MYCOPATHOLOGIA. The Hague. 1960, Mar. 31, v. 12, No. 3, 207–15, 18 figs. [16 refs.] *Candida in vitro* **and** *in vivo*. **1. Clinical Aspects** [WHITTLE, C. H.], 207–11. **2. Experimental Aspects.** [GRESHAM, G. A.], 211–15.

These authors investigated the dimorphism of *Candida albicans* and observed that the yeast or blastospore phase was the characteristic morphological type *in vitro* on standard media whereas the mycelial phase was the characteristic morphological type found in lesions. They showed, furthermore, that in experimentally infected animals the yeast phase was found in abundance in the blood vessels whereas the mycelial phase was predominant in those tissues which were invaded by this organism. *C. J. La Touche*

BRUYT, R. C. Torulosis van het centrale zenuwstelsel behandeld met amfotericine B. [**Torulosis of the Central Nervous System treated with Amphotericin B**] *Nederl. Tijdschr. v. Geneesk.* 1960, July 16, v. 104, No. 29, 1370–73, 1 fig. [21 refs.]

The English summary appended to the paper is as follows:—

"A patient suffering from torulosis of the central nervous system was successfully treated with Amphotericin B. The clinical symptoms of torulosis and its treatment with this new antibiotic are discussed."

OSWALD, Elizabeth J. & POCURULL, Dorothy W. **Comparative** *in vitro* **Effectiveness of Tennecetin and Candicidin Against Selected Fungi.** *Antibiotics & Chemotherapy*. New York. 1960, May, v. 10, No. 5, 285–6.

Tennecetin, described as a "new tetraene antifungal antibiotic" [this *Bulletin*, 1960, v. 35, 122] was compared in activity with the "better known" candicidin in tests of activity against 10 species of fungi, 7 of these being pathogenic in man. The antibiotics were initially dissolved in formamide, and incorporated in concentrations differing 2-fold in slopes of Sabouraud agar. Inoculated slopes were read after 4 days at "room temperature" to determine the fungistatic concentration: "six days later, observations of the same slants were made to determine the fungicidal concentration" [why this concentration could be so determined is unexplained]. There was little difference in activity between the 2 antibiotics: all the species tested were inhibited by concentrations mostly of about 3–25 μgm./ml., and killed by the same or one slightly higher. Tennecetin is considered to be the more fungicidal [but the small differences observed do not give much support to this conclusion]. *L. P. Garrod*

See also p. 1105, ANGIOLI & GORECKI, **Combined Use of Nystatin and Antituberculous Drugs in the Management of Coexistent Fungal-Tuberculous Infections.**

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

MASUNTI, V., MALVENTI, M. & DEL LUCCHESE, L. Ancora un episodio epidemico di tubercolosi polmonare in un centro rurale della provincia di Livorno. [**Another Epidemic Incident of Pulmonary Tuberculosis in a Rural Centre of Leghorn Province**] *Riv. Italiana d'Igiene*. 1960, Jan.–Apr., v. 20, Nos. 1/4, 29–37, 1 fig. [16 refs.] English summary.

The authors refer to a previous paper in which they had dealt with 2 epidemic outbreaks of pulmonary tuberculosis in the rural centre of Castelnuovo della Misericordia, which is in the same province. The outbreak which they now report was within the rural district of Bolgheri, which has 1,534 inhabitants. 400 of these live in the village itself, in old houses which lack satisfactory sanitation and draw an inadequate water supply from artesian wells. The other 1,100 persons are peasant families residing in scattered modern cottages which are said to be adequate. The nearest tuberculosis dispensary is some 20 miles away and public transport is scanty though roads are good.

The authors diagnosed a primary infection in 3 children who attended the dispensary in May, 1958, and later found that 4 other children who had been admitted to the Leghorn Hospital for a pyrexia of unknown origin were similarly affected. There had also been cases of erythema nodosum in the village.

Investigation of other children and family contacts, including mass X-ray examinations and tuberculin testing, showed that there were 26 cases—equivalent to 65 per 1,000 of the population—in the village and that the source of the infection was a 24-year-old schoolteacher who had open tuberculosis with cavitation. 11 of the cases were in schoolchildren and 14 others were family contacts and friends.

The authors also found a peasant woman, aged 44, and a young man, aged 25, who lived in the same house, both suffering from an open infection with cavitation. The woman's disease had been diagnosed as far back as 1952 and she had meantime been under private treatment. Although within the same rural district the house was isolated—some 6 miles from the village—and these 2 open cases are taken to have had no connexion with the outbreak. *J. Cauchi*

HERTZBERG, G. **A Study of the Trends in the Infection Intensity of Tuberculosis in Oslo during 1940–1957.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 1, 1–23, 2 figs.

The author has studied the effect of "tuberculous infection pressure" on the tuberculosis situation in Oslo (population 461,591) during the period 1940–1957. The "pressure" is exercised by infectors on their contacts, some of whom will become infected and develop tuberculosis.

The various factors at work include quantitative changes in the infecting organism, the hosts (infectors and infected), and the environment.

Reports of bacteriological examinations of sputa, gastric contents and laryngeal swabs show that during the period, in spite of an enormous increase in the number of specimens examined, there has been a marked decrease in the number of positive findings. Direct positives fell from 8·7% to 1·8%, and positive cultures from 16·4% to 3·1%.

The incidence of new cases fell from 32·2 per 10,000 to 12·7; the rate of destructive tuberculosis fell from 15·1 to 3·3. In 1944 the rate of new patients with positive sputa was 11·4 and in 1957 it was 2·3. There was thus throughout the whole period a more marked reduction in the incidence of destructive tuberculosis than in the tuberculosis incidence as a whole.

Tuberculin surveys among schoolchildren showed that reactor rates remained practically unchanged during the war (1940–1945) but fell thereafter to 1·7% at 3–6 years, 2·8% in middle school and 4·7% in the highest grade tested in 1957.

The pool of infection has also been reduced by treating at home sputum-positive patients who refused to enter hospital. This has been done with considerable success without bringing about any appreciable dissemination of drug-resistant organisms.

Investigation of the families of new patients showed that where the sputum was positive on direct examination the infection rates in children aged 0–4 years were 59·3 in 1940–1945, 58·5% in 1946–1951 and 53·5% in 1952 1957. This indicates that such patients are almost infectious today as in 1940. *H. G. Calwell*

DEFRU, A. Essai de lutte antituberculeuse en milie rural. (Chefferie des Bayeke.) [**The Control Tuberculosis in the Congo**] *Ann. Soc. Belge Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 71–9 [Numerous refs.]

This work was done in 1956–1958 in the Katanga Province of the Belgian Congo in an area of 5,600 squa kilometres populated by some 9,000 people living in sma scattered communities. Bovine tuberculosis was co sidered to have been virtually eradicated from this are

The programme of control included a tuberculin surv (Mantoux, 10 TU) and examination of suspects, contac and persons known to have had tuberculosis by dire examination of sputum and estimation of erythrocy sedimentation rate. Radiological examination was do in certain selected cases.

There were 3 schools with 1,593 pupils; in boys a girls the reactor rates were 80% and 91% respectively 4 years and 78% and 90% at 15 and over. These rat were 2–3 times higher than those reported in a 19 survey, and they indicate considerable and increasin tuberculosis morbidity in the region. Reactor rates men and women in the villages were 66·3% and 71·6 respectively. Only those showing high degrees of se sitivity were considered to have been infected beyon doubt with the tubercle bacillus.

As public confidence grew the number of perso examined increased as did the number of new cases tuberculosis diagnosed. The number of women patien was greater than the number of men in every villag Different rates of incidence were found in differe localities; the total incidence was 19·77 per 1,000, whic shows that tuberculosis is not a negligible problem rural areas.

Primary lesions amounted to 43·5% of all lesions foun in children aged 0–15 years. It is pointed out that X-ray examination had been used widely a larger numb of cases would have been found. Chemotherapy (isoniaz and PAS) was used when clinical examination suggest that the disease was active.

Tuberculous bronchopneumonia accounted for 20·3 of the lesions in children. 2 children were found to ha tuberculous meningitis. Bone and joint lesions we relatively frequent; the spine was the site most oft affected.

During the course of the survey 136 adults were treat for tuberculosis. Primary lesions were infrequent. Th type of disease seen was similar to that seen in Euro but its behaviour was influenced by factors such anaemia, helminthic infection, malaria and malnutritio Chemotherapy with combinations of streptomyci isoniazid and PAS was generally used and patients we treated outside hospital as far as possible.

The value of BCG vaccination with freeze-dried vacci is described. Vaccination was done by intracutaneo injection. Conversion rates were 72%–77%. The po sibilities of chemoprophylaxis are mentioned.

H. G Calwell

Harvey, C., Rubinstein, C. & Smith, C. E. **A Case-Finding Tuberculosis Survey in Singapore, 1958.** *Brit. J. Dis. Chest.* 1960, July, v. 54, No. 3, 234–46, 6 graphs.

A survey to estimate the incidence of tuberculosis in ngapore was made in 4 months of 1958 with the assis-nce of the Government of Australia. Sample areas timated to contain some 50,000 persons over the age f 14 were selected.

The population of the State was 1,445,930 in 1959, cluding 1,040,570 Chinese, 197,067 Malaysians and 24,083 Indians and Pakistanis. Overcrowding is common the urban area, and tuberculosis is a serious public ealth problem.

54,812 persons were X-rayed, of whom 50,673 were sidents of the districts, and the rest were non-resident. he number of persons found to have active pulmonary berculosis was 2,057, being 3·75% of the population rveyed. Only 322 were previously known to have berculosis. Among the residents there were 1,881 with tive disease, and among the non-residents 176. The ghest incidence was found in Chinatown (4·8%) and e lowest in a Malayan area (1·1%). The incidence males was almost 2½ times that in females; it was 5·6% Chinese males, 2·8% in Malaysian males and 1·3% in dian and Pakistani males. The disease was more preva-nt in the crowded urban areas than elsewhere. The ghest incidence (10·7%) was in males aged 50 and over mpared with 3·6% under the age of 50. The rates females were 2·8% and 1·7% respectively. There was cteriological proof of the diagnosis in 812 patients, ing 35% of the cases. The disease was far advanced 10·8% and minimal in 42·1%.

The occupations of those with active disease were alysed. It was found that the largest group (604) were stly food hawkers, followed by 590 craftsmen and ourers.

By the end of 6 months after the conclusion of the rvey 1,789 patients were being given treatment; 234 had en admitted to hospital and 1,555 were being treated as t-patients.

Some 62% of 1,865 contact children tested with tuber-lin were found to be reactors (Heaf). 36 were con-dered to have active primary lesions but none appeared be ill. These and all reactors under the age of 3 were ven isoniazid as a prophylaxis. *H. G. Calwell*

Koch, H. & Nordin, A. A. **Production of Tuberculin Sensitivity.** [Correspondence.] *Nature.* 1960, July 30, v. 187, 434–5.

Delayed, or tuberculin-type, sensitivity is not trans-able passively by serum but can be transferred with cells of sensitized organisms. It seems to occur inly when the antigen has been phagocytosed.

An attempt was made by the authors to sensitize mals to tuberculin by binding it firmly to phagocytes d injecting the treated cells.

Normal guineapigs were injected intraperitoneally with solution of glycogen in saline, the exudates were lected from the peritoneal cavities 4 days later, and cells (mainly monocytes) were treated as described and incubated with PPD. After washing to remove all unabsorbed PPD the treated cells were injected into the footpads of healthy guineapigs.

12 days afterwards the guineapigs were tested intracutaneously with 250 TU of PPD and the reactions read at 4–5, 24 and 48 hours. The majority had all the characteristics of tuberculin reactions, and were indistinguishable in appearance from the reactions seen in controls which had been sensitized at the same time with living BCG. Similar skin reactions were seen in another group of guineapigs first tested 31 days after sensitization.

Animals with characteristic tuberculin reactions did not show active cutaneous anaphylaxis. Circulating antibodies could not be detected and tests for passive cutaneous anaphylaxis were negative.

Histologically the reactions showed the features of delayed reactions, *viz.* infiltration with mononuclear cells, oedema, absence of perivascular infiltration and scarcity of polymorphonuclear leucocytes. *H. G. Calwell*

Andersen, Shirley R. & Smith, Margaret H. D. **The Heaf Multiple Puncture Tuberculin Test.** *J. Dis. Children.* Chicago. 1960, June, v. 99, No. 6, 764–9, 2 figs. [21 refs.]

Many comparative trials of the Heaf and Mantoux tuberculin tests have been made in the United Kingdom and elsewhere. The present trial was made in a New York hospital. The patients were children aged 1 month to 15 years.

Each patient received a Mantoux test with 5 TU of PPD on one forearm and a Heaf test with glycerinated PPD (2 mgm./ml.) on the other. The degree of Mantoux reaction was recorded in mm. of induration and Heaf's criteria were used to record the degree of reaction to the multiple puncture test. Both tests were read at 72 hours.

A total of 801 clinic and 24 general ward patients were tested. All clinic patients were included who had not been tested within the previous 3 months and were not known to be reactors. In addition 22 patients in the children's tuberculosis ward were tested.

48 patients in the first group reacted to both tests (6·8% of those whose reactions were recorded). 22 patients had doubtful or positive Heaf reactions but negative Mantoux reactions. Of these 17 were tested further with 100 and 250 TU and 13 reacted. This demonstrates the greater sensitivity of the Heaf test compared with the Mantoux test with 5 TU.

The intensity of the positive reactions to both tests was roughly the same in patients with moderate degrees of sensitivity, but with high sensitivity the Mantoux reaction was much more marked than the Heaf reaction. For example a child with 14 mm. of induration (3+) with the Heaf test had 30 mm. of induration with the Mantoux test. Moreover Heaf reactions were less itchy and troublesome than Mantoux reactions.

In the group of tuberculous children the Heaf test followed the same course as the Mantoux in almost every case. The effect of steroids in diminishing tuberculin sensitivity was seen.

The authors concluded that the Heaf test is the best yet proposed for testing large numbers of persons. They

do not think that there is much risk of transmitting the virus of serum hepatitis by the instrument. [See also this *Bulletin*, 1955, v. 30, 294, 668, 669 ; 1956, v. 31, 898 ; 1957 v. 32, 848 ; 1958, v. 33, 451, 938, and 1960, v. 35, 247.]

H. G. Calwell

THURSTON, J. R. & STEENKEN, W., Jr. **Comparison of Gel Precipitin and Sensitized Erythrocyte Techniques for the detection of Antibody in the Serum of Tuberculous and Nontuberculous Patients.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 695–703. [14 refs.]

The authors have tried in this paper to obtain additional data on the reactivity of serum from tuberculous and non-tuberculous patients when tested by a modification of the gel precipitin method used by PARLETT and YOUMANS [this *Bulletin*, 1958, v. 33, 881] and by sensitized erythrocyte tests. Details of the method are given.

The sera from 276 patients were tested. The first table shows that each antigen used was reactive with both tuberculous and non-tuberculous antigens. Of the sera obtained from 73 patients with advanced tuberculosis, 68 reacted to both or either of the tests. 17 of 70 non-tuberculous sera were serologically positive. The differences between the results from various antigens are discussed. The authors conclude that the results are consistent with the known presence of cross-reactive antigens in mycobacterial culture filtrates.

F. H. Young

ALSHABKHOUN, A., CHAPMAN, P. T., WHITE, M. F. & DEGROAT, A. **A Study of the Double-Diffusion Gel Precipitation Test in Tuberculous Patients. With special reference to Technical Problems.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 704–8.

After an antigen which was considered to be satisfactory had been obtained the sera of 885 patients were tested by the double diffusion gel precipitin test described by PARLETT *et al.* [this *Bulletin*, 1958, v. 33, 882]. Only 17% of patients suffering from pulmonary tuberculosis and 25% with non-pulmonary tuberculosis gave a positive result. By using different batches of antigen and dilutions of antigen [the method is described] greatly improved results were obtained. By this method nearly 98% of correct results were obtained. But the immune response that results from continuous re-exposure to tuberculosis is little different from that obtained in active disease. The authors conclude that the test furnishes little information about the extent or activity of the disease.

F. H. Young

DICKIE, A. W. & CREERY, R. D. G. **Infectivity of the Primary Tuberculous Complex. Some Complications in Childhood.** *Brit. Med. J.* 1959, Dec. 26, 1453–4.

Whether it is safe to nurse uninfected children in the same open children's ward as those with childhood tuberculosis of various kinds is in dispute. Most paediatric physicians in the British Isles are prepared to treat such children in open children's wards, but their Scandinavian colleagues do not agree with this.

In 1953 and 1954 a survey was carried out at the Roy Belfast Hospital for Sick Children. During the peric in question 374 children were admitted, and of these 1 had active tuberculosis. 6 had pleural effusions, 1 ha post primary tuberculosis, and 72 had simple or cor plicated hilar adenitis; the remainder had tuberculosis various organs. Routine gastric lavages were not carri out on all these children. In addition 63 children we tuberculin-positive and were presumed to be inactive— following natural infection and 15 following BCG va cination. The method of tuberculin-testing is detailed

Of the 209 children who were tuberculin-negative the beginning, 177 were followed up. No child had co verted at the time of discharge from hospital, and except 16 were re-examined and found to be still tube culin-negative after discharge.

The authors conclude that it is safe to nurse the children in an open ward; and they note that experien has shown that when 1 child in a family develops a p mary complex from an infection outside the home it rare for other children in the same family to develop t disease, unless they have been in contact with t original case. It is very important that the source infection of each child should be found as quickly possible, especially if the infecting individual is likely be visiting the child. It was a practice to ask pare visiting the children not to do so until a clear X-r picture was available. This was arranged on the nig of the admission of the child so that parents could allowed to visit from the following day provided th their chest X-ray films were normal. Other relatives we not allowed to visit the child unless they had norm chest X-ray films.

F. H. Young

GRENVILLE-MATHERS, R., HARRIS, W. C. & TRE CHARD, H. J. **Tuberculous Primary Infection Pregnancy and its relation to Congenital Tube culosis.** *Tubercle.* 1960, June, v. 41, No. 3, 181– [20 refs.]

"Three thousand eight hundred and fifty-five pregna women were tuberculin tested by the multiple punctu test. One thousand five hundred and eighty (41 per ce were tuberculin negative and 1,207 of these were retes later in pregnancy. Thirty-three were found to be po tive at the second test, 2 as a result of BCG vaccinati

"None of the children of these 33 women develo congenital tuberculosis. No tubercle bacilli were cultu from the breast milk or lochia ; but bacilli were cultu from two placentas."

BELL, W. J. **The Initiation of Chemotherapy in P monary Tuberculosis in West Africans. Hospi and Ambulant Treatment compared using Strep mycyclidine-Isonicotinic Acid Hydrazide.** *J. Dis. Chest.* 1960, July, v. 54, No. 3, 247–54, 1 [15 refs.]

Ghanaian males aged 15 to 40 years with pulmon tuberculosis involving more than 1 lung zone and belie to be of recent origin and previously untreated w

dmitted to a therapeutic trial. It was a condition of dmission that the tubercle bacilli present should be fully ensitive to streptomycin and isoniazid. Patients with ıtercurrent disease of such gravity as to affect the prog-osis were excluded.

The patients were allocated at random to an in-patient r an out-patient group. Both received streptomycyli-ene-isoniazid (Streptohydrazid) by injection daily for 2 weeks; the 33 in-patients were confined to bed, and ıe 56 out-patients attended daily for the injection but ontinued their normal activity.

In both groups incidental diseases were treated; all atients were on normal hospital or household diet, and fter the 3 months' period of treatment all continued hemotherapy as out-patients.

The clinical, radiological and bacteriological findings are abulated and analysed. No significant differences were ıown by any of the criteria chosen.

No out-patient failed to report daily for treatment in pite of the considerable difficulty the more seriously ill atients had in travelling. Shortage of hospital beds in Vest Africa denies hospital treatment to many patients ith tuberculosis. The short-term results given above stify out-patient treatment, and further study is to be ade of the effect of prolonged chemotherapy.

H. G. Calwell

ARRAS, T. Note sur l'utilisation du Streptomycilidène isonicotinyl hydrazide (SH) dans la tuberculose pulmonaire. [**The Treatment of Pulmonary Tuberculosis with Streptomycylidene Isonicotinyl Hydrazide**] *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 61–70.

In the conditions prevailing in tropical Africa the ideal eatment for tuberculosis would be a combination of ecific drugs suitable to be given by a single daily or eekly injection.

The majority of the patients treated at the sanatorium Leopoldville have extensive bilateral pulmonary tuber-ılosis ; many are given streptomycin, isoniazid and PAS ıt the only one of the 3 drugs that is taken with cer-inty is streptomycin because it is injected daily. The ıthor has therefore studied the efficacy of a combination streptomycin and isoniazid given in a single injection. reptomycylidene isonicotinyl hydrazide (Streptohydra-d) is stable and water-soluble, containing 1 gm. of reptomycin and 236 mgm. of isoniazid. It is given once ily by intramuscular injection. It was well tolerated the patients in the trial during a period of 6 months.

The trial group comprised 29 patients of whom 26 had estructive pulmonary tuberculosis with cavitation, 2 had iliary disease and 1 had a pleural effusion. Tubercle acilli were seen on direct examination of the sputum in l 26 patients with pulmonary tuberculosis but not in e others; the culture was positive in 23 and negative in Sensitivity tests were done in most cases ; there was rtial resistance to streptomycin in 1 patient and total sistance to isoniazid in another.

4 patients died, 1 in 3 days, 2 in 10 days and 1 after a onth. The 2 patients with drug resistance improved but ill had positive sputa at the end of the 6 months. 23 atients responded favourably as judged clinically and diologically. Sputum conversion occurred in 20.

The use of a preparation such as this would permit out-patient treatment to continue after discharge from hospital with greater ease and safety than when 2 or 3 separate drugs are used.

H. G. Calwell

STOREY, P. B. **A Comparison of Isoniazid-Cycloserine with Isoniazid-PAS in the Therapy of Cavitary Pulmonary Tuberculosis. X. A Report of the Veterans Administration-Armed Forces Cooperative Study.** *Amer. Rev. Respiratory Dis.* 1960, June, v. 81, No. 6, 868–80, 4 figs. [16 refs.]

This is a report of Veterans Administration-Armed Forces Cooperative Study and these studies have the great advantage that as they are carried out at a number of hospitals many extraneous factors are excluded.

Investigation was carried out on 368 patients who were treated with isoniazid and PAS, and 364 who were treated with isoniazid and cycloserine. The 2 groups appear very fairly comparable. All patients had cavitated disease and the sputum contained tubercle bacilli. In both cases the dose of isoniazid was 300 mgm. per day given as 100 mgm. 3 times daily, a dose of cycloserine was 0·5 gm. per day, and that of PAS 12 gm. of the acid or equivalent. No patient who had received antimicrobial therapy previously was included. The patients were assessed at the end of 4 months, and if possible, at the end of 8 months. At the end of 4 months, patients with large cavities treated with isoniazid-PAS showed a substantial improvement (66%) compared with 57% of the isoniazid-cycloserine group.

Treatment had to be changed in 17 patients of the isoniazid-cycloserine group during the first 4 months, and in 27 during the fifth to eighth months; a total of 12%. With the patients on the isoniazid-PAS regime only 2 had to be changed because of failure of treatment during the first 4 months, and 6 during the second 4 months. At the 5–8-month point 78% of the isoniazid-PAS and 68% of the isoniazid-cycloserine group were negative for tubercle bacilli. At the end of 4 months, 7% of the isoniazid-PAS group had resistant organisms against 20·5% of the isoniazid-cycloserine group. At the end of 8 months, 36% of the isoniazid-PAS and 48% of the isoniazid-cycloserine group had resistant organisms to isoniazid. At the end of 4 months, 26%, at the end of 8 months, 30% of patients were resistant to cycloserine. This compares with a pre-treatment figure of 21%. At the end of 4 months' treatment 9% of patients had organisms which were resistant to PAS though in many cases this resistance was only partial. In the PAS group, 30 patients at the end of 4 months, and 8 others at the end of 8 months, had to be removed from the study because of symptoms of drug toxicity. Of the cycloserine patients, 16 were removed at the end of 4 months and 8 at the end of 8 months, because of toxic symptoms.

F. H. Young

DESMEULES, R., DION, R., MOISAN, F. & TURMEL, Colette. **Phenylbutazone and Isoniazid in Pulmonary Tuberculosis.** *Canadian Med. Ass. J.* 1960, June 11, v. 82, No. 24, 1219–22.

The authors call attention to papers reporting satisfactory results from the use of phenylbutazone in patients

suffering from tuberculosis of various types. The paper reports the results on 20 patients—14 female and 6 male—who were suffering from pulmonary tuberculosis mostly of unfavourable types; all had positive sputum although they were afebrile. 17 of the patients had antimicrobial treatment of various kinds, and a list of the type of previous treatment is given. In all cases, phenylbutazone, 400 mgm. divided into 4 doses, was given daily. In 2 patients the phenylbutazone was given alone, as treatment with isoniazid was contra-indicated. In 14 the treatment was combined with isoniazid, and in 4, streptomycin in a dosage of 1 gm. intramuscularly 3 times a week was added. The isoniazid was given at a daily dose of 300 mgm. The only side reaction noted was nausea which occurred in 8 patients. The duration of treatment was between 1 and 12 months according to the case. Reversal of sputum was obtained in 5 cases and radiological clearance in 6.

The authors consider that the use of phenylbutazone is valuable especially in the treatment of certain forms of tuberculosis and is the drug of choice for the relief of arthritis and such disorders in patients with tuberculosis.

F. H. Young

CASSIDY, J. T. & KENNEDY, J. D. **Cystic Cavitation following Chemotherapy of Acute Tuberculosis.** *Irish J. Med. Sci.* 1960, Apr., 6th Ser., No. 412, 153–61, 12 figs.

The authors describe large cystic cavities following the treatment of acute bronchopneumonic tuberculosis with isoniazid. Short case reports are given of 15 cases and in 12 the pathological findings in resected specimens are given. The cystic spaces may be single or multiple usually communicating with the bronchus by a very narrow orifice but in some cases no communication was found. The cavity walls are fibrous and apparently do not contain tuberculous material although the adjacent areas may show resolving tuberculosis. The authors find that when the cavities are large they may bulge out the pleura, and present the appearance of a multilocular cyst; the internal surfaces may be smooth, but in the cases of cavities which are multiple the persistent bronchial and vascular structures in the areas of replaced lung tissue pass around the cavity walls denting them or pass through them as strands which have become progressively thinner as the cavities expand. These cystic cavities appear to be identical with similar lesions which develop during the resolution of staphylococci or suppurative pneumonia under the influence of the commonly used antibiotics. Similar cystic cavities have been noted in lung specimens in 3 cases of sarcoidosis. These cystic cavities are distinguished from chronic cavities with open healing, which may give rise to a similar gross appearance. The cavities are apt to be smaller and single and have a thicker wall, often only partially epithelialized. The excavation of bronchial cold abscesses described by CLEGG may give rise to a saccular smooth-wall cavity completely lined by bronchial epithelium.

Tuberculous bronchiectasis arising in a collapsed lobe may give rise to the formation of diffuse smooth-walled saccules; these all communicate directly with the bronchi. Finally the congenital cyst in the lungs described by HEAD (*Amer. J. Surgery*, 1955, v. 89, 1019) and others are re ferred to. Bronchography was performed on most of th 15 patients but in only 1 did the contrast medium ento the cavity. It also demonstrated constant bronchiectat dilations surrounding the cyst. The outlook for thes post-antibiotic and cystic cavities is not known but i only 1 was the sputum found to be positive pre-opera tively, subsequently becoming negative: usually th sputum remains completely negative. The cavities de cribed are unstable and may increase in size. In n case has there been evidence of a breakdown of th tuberculosis in connexion with these cavities.

This paper is interesting in that it purports to fin the difference between the cavities described and th ordinary cavities produced by open-healing which als appear to be cystic in character, but are smaller tha those described in this article. *F. H. Young*

BEARD, H. J. **250 Cases of Resection for Pulmonar Tuberculosis.** *Brit. J. Dis. Chest.* 1960, July, 54, No. 3, 265–71.

This paper is a report on the first 250 cases of rese tion for pulmonary tuberculosis performed in Kellir Hospital, Norfolk, between March 1950, and Augu 1957. The indications for various types of resection an discussed.

Pneumonectomies were performed on 60 patients wit 9 operation deaths; lobectomies on 86 with 5 deaths, an segmental resections on 104 patients with 2 operatio deaths; there were 7 later deaths. The chief causes c death were broncho-pleural fistula and empyema. 1 patients, of whom half were sputum positive at the tim of operation, later had a relapse of their disease. Com plications occurred mainly during the first 4 years whe chemotherapy was inadequate. 3 deaths were due t pulmonary embolus. For some reason or other pu monary emboli are far more likely to occur in resectio operations than thoracoplasties.

[It is a pity that in so many of these reports on a serie of resection cases those who had adequate pre- and pos operative chemotherapy are not clearly differentiate from those who had not. The prognosis both as regard death and relapse seems very different in the 2 types c case.] *F. H. Young*

WEBB, W. R., WOFFORD, J. L. & STAUSS, H. K. **Re sectional Therapy for Residual Noninfectiou Cavitary Tuberculous Lesions.** *Amer. Re Respiratory Dis.* 1960, June, v. 81, No. 6, 850–5 3 figs. [14 refs.]

This paper is a contribution to the controversy as t whether non-infectious cavitary lesions in pulmonar tuberculosis should be resected. 200 operations we performed on 188 patients; only those were included wh had pathological demonstration of air-containing caviti regardless of the pre-operative X-ray interpretatio Bronchiectatic lesions of one kind or another are n included. All bacteriological studies of sputum an gastric washings for at least 2 months before operati were negative. Of the 188 patients, 130 were receivi initial antimicrobial treatment, and 58 re-treatment. C

the 7 deaths, only 1 was attributable to active tuberculosis; the details of these are given. There were 26 pneumonectomies, 91 lobectomies (with 23 in whom more than one lobe was resected); 58 segmental resections, and 2 wedge resections. Reactivation occurred in 14 patients. 175 patients (93·1%) are alive and well.

Acid fast bacilli were demonstrated in 42·5% of the resected specimens. Anti-microbial therapy was discontinued 1 year post-operatively in nearly all cases. It was noted that reactivation was uncommon if the cavities were thin-walled; this division is not made in the quoted figures.

The authors point out that these results are better than those reported in groups of cases of a similar character treated by long term antimicrobial treatment. They conclude that resection should be carried out in this type of case unless there is a good reason to the contrary.

[This is a sound paper, but it is a pity that the thick-walled and the thin-walled cavities are not dealt with separately, as it is in the thin-walled cavity cases that the clinician's difficulty occurs most often.]

F. H. Young

Angioli, G. & Gorecki, Z. **Combined Use of Nystatin and Antituberculous Drugs in the Management of Coexistent Fungal-Tuberculous Infections.** *Canadian Med. Ass. J.* 1960, June 18, v. 82, No. 25, 1274–5. [10 refs.]

The authors suggest that there is a frequent tendency for tuberculous disease to pursue a more devastating course as a consequence of fungal infection. Certain pathogenic strains of *Candida albicans* contain or produce a factor which promotes the growth of tubercle bacilli *in vitro*. In a recent analysis by Longo 135 out of 505 newly admitted tuberculous patients showed a coexistent infection of tubercle bacillus and *Candida* species, and of these *Candida albicans* was present in 100. This paper describes the use of nystatin in conjunction with antituberculous drugs in the treatment of tuberculous patients with evidence of coexistent fungal infection.

23 patients in whom cultures of tubercle bacilli were obtained from the sputum or bronchial washings showed fungi in some of the material obtained from the patients. In 18 patients the fungus isolated was identified as a species of *Candida*. Nystatin was administered in a dosage of 500,000 to 1,000,000 units per day, along with the usual dosages of one or more antituberculous drugs. The combined therapy was maintained for periods of 3 to 21 months. 11 of the 13 patients who had tubercle bacilli in the sputum at the beginning of the study became negative while 10 initially negative remained so. 18 were clear of fungi and in 16 patients clinical and radiological improvement was observed. In 3, little improvement occurred, 1 showed no change, and 3 patients succumbed. No instances of intolerance or undesirable reactions with use of nystatin was observed. A table giving a summary of the data on the 23 patients is appended, and 3 representative cases are described. The authors suggest that the oral administration of nystatin and antituberculous drugs offers a much improved progress where there is coexistent fungal infection, particularly when it is due to species of *Candida*.

F. H. Young

Holm, S., Rasmussen, K. N. & Winge, K. **Relapse among Patients with Pulmonary Tuberculosis in Copenhagen in the Years 1945 to 1958.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, Nos. 3/4, 235–47, 1 fig. [10 refs.]

A study of the incidence of relapse in pulmonary tuberculosis is complicated by the fact that different authors use a different definition for the term "relapse". In this paper from the Central Municipal Tuberculosis Dispensary, Copenhagen, the authors lay down clear criteria defining what they mean by "relapse". In brief, this means a deterioration in a patient who for 3 years has had no radiological change, no positive sputum by microscopy or culture, and has been regularly under observation prior to the deterioration.

In an analysis of 1,379 cases, 668 patients, representing 693 cases of relapse, fulfilled the requirements. In 66 of these patients the initial condition had the character of primary tuberculous infection. Tables are given showing the sex and age at the time of first diagnosis, interval between the diagnosis and the commencement of the stationary phase, and the extent of the lung lesions at the time of first diagnosis. As the years went by the numbers of cases of relapse steadily decreased, but the decrease was slowed down in the period 7–14 years by the increased care taken in the culture of the sputum. A number of cases had to be designated as "relapsed" merely because positive cultures were obtained in patients who were apparently radiologically and clinically quiescent. Of the relapses, 48·9% had X-ray progression and a positive sputum examination, 39·1% had a positive sputum examination, but an unchanged X-ray picture, and 11·9% X-ray progression with a negative sputum, but in the last group tubercle bacilli were subsequently found in sputum or gastric contents. Only 53 patients were treated with chemotherapy, the majority for less than 6 months.

In 168 patients the sedimentation rate was found to be over 20 mm. during the 6 months before the relapse occurred.

The proportion of patients who had social circumstances of an unfavourable character was considerable. 11 patients had diabetes at the time of the relapse and 12 had gastric ulcers before or during the stationary phase.

F. H. Young

Alling, D. W. & Bosworth, E. B. **The After-History of Pulmonary Tuberculosis. VI. The First Fifteen Years following Diagnosis.** *Amer. Rev. Respiratory Dis.* 1960, June, v. 81, No. 6, 839–49, 5 figs. [12 refs.]

This paper continues the study on the after-history of persons with pulmonary tuberculosis, previously described for the first 10 years following diagnosis [see this *Bulletin*, 1954, v. 29, 468, 930, 1220; 1955, v. 30, 301, 674]. The clinical material includes all confirmed cases of active pulmonary tuberculosis diagnosed among residents in upstate New York during the years 1938 to 1948, inclusive.

564 persons are dealt with. The statistical method is the anniversary method described in this series of papers.

Statistical tables are given showing age, sex, progress, type of disease, and their fate. Graphs are given which bring out the principal points and enable the reader to grasp them without referring to the rather elaborate tables. It is interesting to note the rather high proportion of relapses in the minimal type of tuberculosis in the early years. *F. H. Young*

BERNARD, E. & CROS-DECAM, J. La vaccination BCG par voie buccale chez l'enfant du premier age. [**Oral BCG Vaccination of the Newborn**] *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 21/22, 418–22, Discussion 422–8, 2 graphs.

The French National Academy of Medicine recommends that infants be vaccinated with BCG as early as possible. At present the vaccination is compulsory only from the age of 6 years and the only infants vaccinated are contacts of tuberculous patients and those in institutions or fosterage.

Tuberculin surveys have shown that some 200,000 children in France have contracted a natural tuberculous infection by the age of 6, and in 1958 174 children died of tuberculous meningitis. In this situation it is considered desirable that infants be vaccinated.

The vaccination with BCG of newborn infants is just as successful as that of older children, and the immediate neonatal period (after birth weight has been regained) is the most suitable time for doing it.

The authors vaccinated 500 infants orally with 2 doses of BCG with an interval of 5 days between them. Both freeze-dried and fresh vaccine was used. The dose was 50 mgm. up to 8 months, 75 mgm. from 9 months to 2 years and 100 mgm. after 2 years. The conversion rate was 91–98%, and the degree of post-vaccinal sensitivity was similar to that found after parenteral vaccination. Regional adenitis (cervical) occurred occasionally but never with freeze-dried vaccine.

At present the only methods of BCG vaccination approved by regulation in France are intracutaneous injection and scarification. The Academy recommends that oral vaccination be similarly approved.

GUÉRIN recalled that BCG vaccination orally was the original method of CALMETTE.

GERNEZ-RIEUX presented a follow-up of the original vaccinations done in Roubaix in 1925–1934 demonstrating long-continued protection by BCG [this *Bulletin*, 1960, v. 35, 778]. He also mentioned the favourable results presented at the Congress of the International Union Against Tuberculosis in Istanbul in 1959.

H. G. Calwell

MAGNUSSON, M., JESPERSEN, A. & WEIS BENZTON, M. **Revaccination with BCG Vaccine. An Experimental Study in Guinea Pigs.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 1, 34–56, 8 figs. [44 refs.]

Revaccination with BCG is usually recommended when the tuberculin sensitivity conferred by a previous vaccination has disappeared. It is not however certain whether disappearance of sensitivity indicates disappearance of immunity or whether the degree of immunity conferred by revaccination is greater or less than that conferred by earlier vaccination.

The authors have investigated these matters experimentally in guineapigs. Details of the experiments are given. The animals were vaccinated intracutaneously with 0·075 mgm. of fresh Danish BCG and the local reactions were recorded. PPD (5 TU) was used for testing sensitivity or for sensitizing. The animals were challenged with virulent bovine tubercle bacilli (2,000 viable units) and allowed to die of tuberculosis spontaneously. The length of survival after challenge was used to measure the degree of immunity.

Comparison of the local reactions to original and subsequent vaccination 7 months after the first showed that the majority of the revaccinated animals had larger reactions than those primarily vaccinated (Koch reaction). Even 9 months after primary vaccination revaccination caused a weak Koch reaction in several animals. The Koch reaction was found oftener if after the primary vaccination the animals had been sensitized further by tuberculin testing or revaccination.

The gradual waning of post-vaccinal tuberculin sensitivity was demonstrated by tests done 2, 5 and 9 months after vaccination.

All the groups of vaccinated animals survived longer on average than the unvaccinated controls. In spite of waning or absent tuberculin sensitivity animals vaccinated 9 months before challenge were found to possess the same degree of immunity as those vaccinated only 2 months before challenge. Revaccination increased immunity and was followed by slightly less tuberculin sensitivity than primary vaccination.

"The present work indicates that, where an increase in resistance is desired, it is justifiable to revaccinate when the tuberculin sensitivity induced by the primary vaccination has waned. On the other hand, however, it would not seem to be necessary to revaccinate at this stage, since some acquired resistance still persists."

H. G. Calwell

JOOS, H. & PULVER, W. Zur Diagnose und Prognose der Meningitis tuberculosa. [**The Diagnosis and Prognosis of Tuberculous Meningitis**] *Schweiz. med. Woch.* 1960, Aug. 6, v. 90, No. 32, 842–50, 8 figs. [Numerous refs.]

The diagnosis of tuberculous meningitis can still present difficulties, sometimes because of the absence of unequivocal evidence of tuberculosis or perhaps because of the concurrent outbreak in the neighbourhood of some other kind of meningitis. However, increasing knowledge of other non-purulent forms of meningitis especially those due to virus infection has led to improved differential diagnosis. New methods of investigation have also assisted.

The authors treated 68 patients with tuberculous meningitis in the period January 1950 to July 1959. 40 were male and 28 female. The numbers seen yearly fluctuated widely and irregularly between 12 and 3. 1951 was the best complete year and 1957 almost the worst.

19 patients were aged 0–9 years, 12 10–19, 18 20–39, 16 40–59 and 3 were aged 60–69 years. The highest seasonal incidence was in Spring.

21 patients died (30·8%); the highest death rate was

in children aged 0–4 years, 12 of the 21 patients died within 30 days of the beginning of treatment.

The source of infection was found inside the family in 7 cases and in the neighbourhood in 1. 21 of the patients had been under treatment for other manifestations of tuberculosis before the onset of meningitis. None of the patients had been vaccinated with BCG.

The importance of early diagnosis was shown by the fact that of 28 patients in whom there was early diagnosis 7 died compared with 14 of 40 in whom the diagnosis was late. Another important matter was the state of consciousness on admission. 6 of 37 patients fully conscious on admission died compared with 15 of 31 with impaired consciousness.

63 of the patients were tuberculin reactors; of the 5 non-reactors 1 had previously been treated for tuberculosis and 4 had manifestations of tuberculosis other than meningeal. Tubercle bacilli were found in the cerebrospinal fluid of 3 of these, and the diagnosis was confirmed at post-mortem examination of the 4th.

Concomitant tuberculous lesions were found in 66 patients including primary pulmonary complex (15), miliary disease of lungs (18), choroidal tubercles (10), pleural effusion (5), post-primary pulmonary tuberculosis (12) and extrapulmonary lesions (11).

The findings in the cerebrospinal fluid on admission included leucocytosis in every case, high globulin content in 98·5%, decreased chloride and sugar content in 74 and 78% respectively and coagulation on standing in 66%. Tubercle bacilli were found on direct examination in 28% and by culture or inoculation tests in 38%.

The favourable effect of isoniazid on the outcome was shown. 15 of 25 patients who did not receive isoniazid died compared with only 6 of 43 patients who were given isoniazid. *H. G. Calwell*

HORWITZ, O. **Lupus vulgaris cutis in Denmark 1895–1954. Its Relation to the Epidemiology of other Forms of Tuberculosis. Epidemiology and Course of the Tuberculous Infection, based on 3902 Cases from the Finsen Institute, Copenhagen.** *Acta Tuberculosea Scandinavica.* 1960, Suppl. 49, 142 pp. + numerous pp. of tables, 36 figs. [Numerous refs.] [Also obtainable as bound volume price $6.50 from Finsen Institute, Copenhagen.]

The Finsen Institute, Copenhagen, is a nation-wide centre for the treatment of patients suffering from lupus vulgaris in Denmark. Its records form the basis of this study which concerns 3,902 patients admitted for treatment in the period 1895–1954. This number was estimated to represent more than 80% of all cases diagnosed in Denmark during the period stated. Males numbered 1,140 and females 2,762.

The clinical characteristics of lupus were present in most cases; in addition the diagnosis was confirmed bacteriologically in 7% of the male and 5% of the female patients and histologically in 24% and 21% respectively.

The incidence of lupus fell from 44 per million males and 114 per million females in 1899 to 2 and 4 respectively in 1950–1954. There was a rise in incidence during the war of 1914–1918, and the fall was interrupted in 1939–1945. A tendency to an increasing incidence was seen in the period 1950–1954; this may have been the result of improved diagnostic facilities in the provinces.

In females the incidence was on average 2·4 times that in males, and generally the relative difference in incidence has been more or less constant. For the entire period the incidence in males was highest in Copenhagen (15% higher than in the rural areas), while in females there was no definite difference between capital, town and country. Within each region females had a higher incidence than males — 2·0 times higher in Copenhagen, 2·5 times higher in provincial towns and 2·4 times higher in rural districts.

It was possible to distinguish 6 geographical regions with varying incidence. These are illustrated on a map. The rates in the south and north-western regions were 2–3 times higher than in the eastern region.

During the period 1921–1954, for which the incidence of pulmonary tuberculosis is known, the ratio of patients with lupus to patients with notified pulmonary tuberculosis was 1:100 in males and 2:100 in females. Since the 1930 decade the incidence of lupus has fallen more rapidly than that of pulmonary tuberculosis. This could be due to the pasteurization of milk and the eradication of bovine tuberculosis but it could also be due at least in part to the increased scope of mass radiography. There was found to be striking agreement in the geographical distribution of lupus, pulmonary tuberculosis and bovine tuberculosis.

During the present century the total prevalence of lupus rose slowly to a flat peak in the 1930's when it was about 350 per million males and 800 per million females. Thereafter the respective rates fell to 250 and 525.

The proportion of patients in the older age-groups increased during the period; in 1904 60% of the males and 35% of the females were under 25 but in 1954 only a small number were under 25. The age patterns for lupus and pulmonary tuberculosis showed a similar structure with peaks at the same ages, and both showed a relatively greater decline in the rates in young than in old people. The greatest difference between the 2 diseases was that with lupus the incidence was higher in females than males at all ages; the relative difference increased with age.

The duration of lupus at the time of admission was examined. In patients under 25 it was less than 2 years in 35–40%, and in practically none was it over 21 years. Among patients aged over 25 years at admission the duration was less than 2 years in 20–30% and 21 years or more in 20–30%. The median duration in young patients was around 3 years and in older patients around 6–10 years. In young patients the distribution was almost identical in both sexes but in older patients there were relatively more cases of short duration among the females.

The types of tubercle bacilli were studied in 214 patients. It was not possible to evaluate the frequency of bovine strains. Bacilli of human type were present in the majority of the patients.

The outlook as far as survival is concerned was favourable for patients in whom lupus was the only form of tuberculosis; their death rate was the same as that of the general population. Most of the patients, however,

suffered from other forms of tuberculosis in addition to lupus, and in their case, particularly if pulmonary tuberculosis was present, the death rate was much higher than in the general population. Children and young persons especially fared badly. In 39% of male patients and 31% of female patients, the cause of death was tuberculosis.

Lupus was the only tuberculous disease in 24%, while other forms of tuberculosis occurred in 76%. Glandular tuberculosis and lupus of mucous membranes occurred in 40% and tuberculosis of the respiratory system, of bones or joints, and other forms of skin tuberculosis in 10–20%. The public health aspect of lupus is indicated by the high frequency of infective forms of tuberculosis in the patients. Within individual age-groups the incidence of respiratory tuberculosis was about 5 times higher than in the general population. *H. G. Calwell*

VENEREAL DISEASES

World Health Organization. Technical Report Ser. No. 190. **Expert Committee on Venereal Infections and Treponematoses. Fifth Report.** Geneva, 21–26 September 1959. 73 pp., 1 fig. [Refs. in footnotes.] 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [5s.; $1.00; Sw.fr. 3.–.]

This committee, which consisted of experts from different countries, issued its fifth report. It first considered the Brussels Agreement and recommended WHO to encourage more maritime countries to ratify it, laying particular stress on minimum standards for VD management in seafarers; appendices set out "definitions" (of VD services, staff equipment, etc.), training of personnel and equipment.

Section 2 deals with venereal infections, especially syphilis and gonorrhoea; the former is still common in some countries, notably in Asia and South America, and notification of cases leaves much to be desired; gonorrhoea needs special methods of control and the neisseriae demand research, as does non-gonococcal urethritis.

The third section deals with the eradication of endemic treponematoses, especially yaws and pinta; the recommended dosage of penicillin is laid down as 1·2 mega units of PAM for treatment of active disease and half this for latent cases and contacts; it is pointed out that improved social conditions also help; the danger of the endemic form being replaced by venereal syphilis is stressed; the prevalence of this latter disease should be studied by serum testing of unselected pregnant women. Penicillin reactions are considered at some length; these are divided into (1) the rare life-threatening reactions such as anaphylaxis, exfoliative dermatitis and serious super- and cross-infections, and (2) non-serious and mild eczematous and urticarial reactions. The incidence of fatal anaphylactic reactions is estimated at about 1 per million injections and of non-fatal anaphylactic reactions at about 10 times this figure; known deaths are estimated at 90–115 per annum throughout the world. Reactions seem to be increasing—from 5·95 per 1,000 VD patients treated in 1954 to 9·96 in 1959 in surveys in the USA. Sensitizing factors are important and may be caused by penicillin-contaminated milk, syringes, dust and virus vaccines. Preventive measures should be taken at the public health and patient level; stopping the misuse of penicillin and taking precautions before (history taking) and after administration; much research is needed into the nature of sensitizing reactions.

Of drugs for use when penicillin is contra-indicated for the treatment of treponematoses, chlortetracycline, oxytetracycline, tetracycline, chloramphenicol, erythromycin and carbomycin are the most promising; these all cause dark-ground negativity in 18–72 hours, bring about rapid healing of lesions and, as far as information goes, seem to give a satisfactory serological response (especially erythromycin and carbomycin). They are however not free from side effects and are more expensive than penicillin; it is recommended therefore that an endeavour should be made to find a preparation which is safe, inexpensive and quickly acting for use in public health programmes.

There is a comment on international standardization of PAM and benzathine penicillin, reference preparations of cardiolipin and lecithin, and human syphilitic serum.

The serology of the treponematoses is becoming very complicated with the introduction of new tests; of these the RPCF (Reiter protein complement fixation) holds out considerable hope while the RPR (rapid plasma reagin) and the PCT (plasmacrit) should be studied with a view to their use in tropical conditions for mass testing. Research in addition to that on the gonococcus should be directed to studies of the treponeme, particularly to culture of virulent organisms, and to their antigenic structure; the epidemiology, pathology, clinical manifestations (especially cardiovascular and neurological), diagnosis, treatment and prevention of the treponematoses all call for further study.

Exchange of information would be furthered by the proposed International Conference on yaws and the proposed International Symposium on venereal diseases in 1961 and 1962 or 1963 respectively.

There is still need for standardization of nomenclature of syphilis and yaws, for the training of doctors and technical assistants in these subjects and for intensification of health education and instruction about VD including family education of "teenagers".

There are 2 annexes, one showing the form used for area resurvey returns (where a yaws campaign has been carried out) and one giving a general review of research needed into the treponematoses.

[For the fourth Report, see this *Bulletin*, 1953, v. 28, 815.] *T. E. Osmond*

KEIGHLEY, Elizabeth. **Venereal Disease among Women Prisoners.** *Lancet.* 1960, July 30, 253–4.

Of 2,382 women in Holloway prison, London, examined in 1958, 31 had syphilis, 215 gonorrhoea and 778 other conditions requiring treatment. In that year prostitutes admitted numbered 464 compared with 292 in 1957 and 201 in 1956; in 1958, 36% were under 20 years of age; of 415 who were examined, 23 had syphilis, 137 gonorrhoea and 230 had a vaginal discharge; of 145 teenagers, 4 had syphilis and 71 had gonorrhoea. Thus it appears that venereal disease is common among women prisoners and particularly so among the younger ones, most of whom appeared to be both ignorant of the fact, and callous. Section 26 of the Criminal Justice Act of 1948 proved helpful in ensuring examination, treatment and rehabilitation, but the Street Offences Act of 1959 may hinder the detection of venereal diseases by causing prostitutes to leave the streets and adopt the "call-girl" system. *T. E. Osmond*

SIMPSON, W. G., HARRIS, A., GARSON, W. & BUNCH, W. L., Jr. **The Reiter Protein Complement Fixation Test as a Diagnostic Aid in Syphilis.** *Arch. Dermat.* 1960, June, v. 81, No. 6, 904–7, 3 figs.

In 1958, 204 sera, 121 from old syphilitics and 83 from controls, were retested after 25 years. In 56 untreated syphilitics, average age 69, duration of infection 43 years, treponema pallidum tests (TPI, TPCF, FTA and tpcf-50) there were 70–93% of positive results; the corresponding figures for 2 Reiter protein tests (RPCF and KRP) were 42–61 and for 4 non-treponemal tests (USR-11, Kahn, Kolmer and VDRL) 43–50. Thus it is seen that the Reiter protein tests reverse to negative in much the same way as the non-treponemal tests.

In a second series of syphilitics treated with small amounts of arsenicals (average age 58, duration of infection 36 years), reactivity ranged from 75 to 89% in treponemal tests, from 22 to 47% in Reiter protein tests and from 9 to 54% in the non-treponemal tests; presumably the fall in reactivity was caused by treatment.

Of 83 controls all were negative with Kahn, Kolmer and VDRL but 2% were reactive with KRP and 16% with TPCF. The main value of the Reiter protein tests seems to lie in the non-syphilitic and biologically false positive cases. Of 2 previous series (1) of 117 false positive sera previously negative to TPI, this test gave 4% of reactions, KRP 7% and VDRL 42%; (2) of 117 sera clinically biologically false positive, TPI was reactive in 30%, KRP in 34% and VDRL in 28%.

Because it costs only a few cents, compared with 30 dollars for TPI, the Reiter protein test is frequently used instead, but it must be stressed that in long standing syphilis it may be expected to be negative in more than 50% of cases. *T. E. Osmond*

OBEID-RUGGLI, V. M. E. Über Resultate der Penicillinbehandlung der Syphilis mit einer protrahierten Kur von 14,4 Millionen Einheiten. [**Results of Prolonged Treatment of Syphilis with Penicillin in a Total Administration of 14·4 Million Units**] *Schweiz. med. Woch.* 1960, July 30, v. 90, No. 31, 820–26. [17 refs.]

This is a detailed account of the results observed in syphilitic patients most of whom had received a single course of penicillin treatment in the period 1948–55. The method of treatment adopted in the 2 institutes in Zürich was to give 3 intramuscular injections of 0·6 million units of procaine penicillin weekly for 8 weeks, which is a total amount of 14·4 million units. 191 patients were treated in this period who had had no previous specific treatment and of these 107 remained for assessment 3½ to 8 years later. The composition of this group was: primary syphilis 20 cases, secondary 21, tertiary syphilis 3, neurosyphilis 11, latent syphilis 47 and congenital syphilis 5 cases.

The clinical and serological findings at re-examinations are fully described and the main conclusion is that this method of treatment is good although it is realized that an observation period of 3–10 years is not long enough to allow of a final judgment. In no instance was there any clinical relapse in this group of 107 patients. In all patients with syphilis I and II clinical and serological cure was effected and in all but 1 of these patients by a single course of treatment. In the cases of late syphilis, however, complete return to normal values of the serological tests was not always obtained even after repeated courses of treatment. *M. E. Delafield*

CATTERALL, R. D. **Diagnosis and Treatment of Trichomonal Urethritis in Men.** *Brit. Med. J.* 1960, July 9, 133–15. [14 refs.]

The incidence of trichomonal urethritis has been variously estimated as from 5 to 68% in males suffering from non-gonococcal urethritis but it is suggested that it is higher than is commonly supposed. Investigation was by smears from the urethra, cultures and examination of centrifuged urine [no mention is made of prostatic secretion]. *Trichomonas vaginalis* was found in 126 out of 2,300 cases (5·5%). Signs and symptoms were usually mild or were absent; 71·4% complained of urethral discharge. *T. vaginalis* was found in urethral scrapings in 88·8% and cultures were positive in 58 out of 63 cases (92%): the organism was found in 85% of sexual partners.

Treatment was only moderately satisfactory; irrigations with potassium permanganate, oxycyanide of mercury or Dequadin [dequalinium chloride] were apparently successful in 59–73%. Some systemic form of treatment may offer the best hope of cure [see this *Bulletin,* 1960, v. 35, 991]. Failure of treatment may be due to urethral stricture and reinfection appears to be common unless the sexual partner is also treated. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

PROCEEDINGS OF A SYMPOSIUM ON IMMUNIZATION IN CHILDHOOD [BOYD, J. S. K., Chairman]. Held in the Wellcome Building, London, 4th to 6th May 1959. 139 pp., 5 figs. 1960. Edinburgh. London: E. & S. Livingstone Ltd., 48 Bloomsbury Street, W.C.1.

Although this symposium was sponsored by the Wellcome Foundation, it was organized by an independent steering committee under the chairmanship of Sir John BOYD. The declared object of the conference was to consider the accumulated knowledge available about immunization in childhood, especially with regard to diphtheria, tetanus, pertussis, smallpox and poliomyelitis, to attempt to resolve conflicting views and to recommend acceptable immunization programmes for children up to school-leaving age for general use in Great Britain.

There were some 70 participants, the majority of whom were British but there were also distinguished representatives from the United States, France, Commonwealth Countries and WHO. All the participants were actively concerned with some aspect of immunization and most of them had long experience of the subject in their own particular field. The conference was divided into 5 sessions: the first was devoted to the consideration of the risks of immunization; the second to vaccination against poliomyelitis and pertussis; the third to diphtheria and tetanus immunization, the use of combined prophylactics and the maintaining of personal records of inoculations; the fourth discussed the pros and cons of immunization programmes and the final session considered the various recommendations put forward, and formulated an agreed inoculation programme.

Each session opened with appropriate papers but in most cases these were brief and designed to promote discussion rather than to attempt to present new information. The opening speakers answered questions and summed up at the end of each discussion and before the opening of the last meeting the steering committee discussed with the various session-chairmen the results obtained and formulated draft recommendations for further discussion and agreement at the final session. The draft recommendations were slightly modified as a result of these discussions and the symposium finally adopted two schedules of immunization. The essential difference between the two schedules being that one used pertussis vaccine as a separate prophylactic during the first 6 months of life whereas the other schedule used triple prophylactic (diphtheria-tetanus-pertussis) during the same period.

Schedule A recommends 3 doses of pertussis vaccine between the age of 5 weeks and 6 months with a minimum interval of 4 weeks between the doses. 2 doses of poliomyelitis vaccine at 7–10 months with an interval of 4 weeks followed by 2 doses of diphtheria-tetanus prophylactic at 10–12 months, the interval between the two doses again being 4 weeks. At the time of the second dose of diphtheria-tetanus a fourth dose of pertussis is given in the opposite arm. At 15–18 months third doses of diphtheria-tetanus prophylactic and poliomyelitis vaccine are given at the same session into opposite arms. Smallpox vaccination may be done at some convenient time during the first 5 years. At school entry a fourth dose of diphtheria-tetanus toxoid is recommended and a further dose at 8–9 years, at which time it would also be suitable to re-vaccinate the children against smallpox. Children exposed to special risk of tuberculosis will already have received BCG vaccine, but all children aged 10–15 years should be tuberculin-tested and negative reactors vaccinated.

Schedule B. During the period 2–6 months the infant is to be given 3 doses of diphtheria-tetanus-pertussis (triple) vaccine with a minimum interval of 4 weeks between the doses. 2 doses of poliomyelitis vaccine at an interval of one month are given at 7–10 months and this is followed by a third dose at 15–18 months when the fourth dose of the triple vaccine should also be given; these are administered at the same vaccination session but in opposite arms. From then onwards the schedule is similar to that laid down in Schedule A.

Several other agreed recommendations were made, the most important of which were concerned with personal records of immunization and the employment of a sterile syringe and needle for each injection made (p. 129). While fully recognizing the importance of a readily available personal record of immunization, especially against tetanus, the meeting could hardly do more than offer a number of valuable suggestions about the form it should take. One of the opening papers at the first session (by J. W. HOWIE, pp. 21–22) dealt with the sterilization of syringes and it provoked a discussion that continued, on and off, throughout the conference. Everybody agreed that the provision of a sterile syringe service, operating from the various hospital centres, or the national provision of sterile disposable syringes and needles was the ideal, but there was a reluctance on the part of some to agree that no other methods could be accepted. There was a reasonable hope that the development of a satisfactory disposable syringe in a suitable pack at an economic price would not be long delayed and this would appear to offer a solution to a problem which faced those working away from centres where a sterile syringe service could be readily organized.

Particular prophylactic preparations received due consideration during the different discussions but the main business of the conference was the formulation of agreed vaccination programmes. It was constituted for this purpose and it would appear from the well set-out proceedings that the object was achieved in an orderly and satisfactory manner. It may be of interest to record, for instance, that in the special session devoted to immunization against poliomyelitis, although the living attenuated vaccine was discussed by several speakers, it was not a major issue. Most of the participants were obviously

referring to their studies with formalin-inactivated vaccines, but without going deeply into technical details it was clear that there were still many problems yet to be solved with regard to protection against poliomyelitis, and that these were more concerned with the actual vaccine preparation than the immunization programme.

H. J. Bensted

REV. D'IMMUNOLOGIE. 1960, Jan.–Mar., v. 24, Nos. 1/2, 1–344, illustrated. [Numerous refs.] Calendrier des Vaccinations. **[Immunization Programmes]** Séminaire organisé par le Centre International de l'Enfance sous la présidence du R. DEBRÉ.

The entire January-March issue of this journal is devoted to an acount of the conference held in Paris in October 1959 on the immunization of young children. The conference was attended by just over 130 recognized authorities on the subject, mainly from the Western European countries but several of the Eastern European countries were also represented. In addition there were delegates from Great Britain and the United States of America but as would be expected quite half the participants came from France. It will be recalled that a very similar conference was held some months previously in London. (*Brit. Med. J.*, 1959, v. i, 1342, and *Proceedings of Symposium on Immunization in Childhood*, see above.) There was also a series of articles on the same subject in the December 1959 issue of *Ann. Inst. Pasteur* [this *Bulletin*, 1960, v. 35, 571 *bis*, 581, 585 *ter*]. Although there are many differences in the detail of what was said at the two symposia and in the method of approach of the various main speakers the two meetings were very alike in organization, conduct and substance.

The proceedings of the Paris symposium now published in the *Revue d'Immunologie* are very comprehensive and well set out and carefully prepared. There are 4 main sections—basic immunity, immunization with various forms and combination of vaccines, immunization against virus diseases, duration of immunity and programmes of immunization procedures.

The symposium opened with a paper by B. VAHLQUIST (Sweden) on the transfer of immunity from the mother to the infant through the placenta and also through breast feeding (pp. 3–12). This stimulated a fair discussion in which some 12 of those attending took part, among whom L. NICOL, O. GIRARD, R. CORVAZIER, M. CHEYROUX, P. RECULARD and P. SIZARET (pp. 16–23) and R. BACKHAUSZ and G. LENART (pp. 23–27) gave prepared papers, the latter, dealing with the elimination of antibody from replacement transfusions, being of some interest. The president, Professor R. DEBRÉ, took part in this discussion. At the end of the session the opener Vahlquist adequately dealt with the various questions put to him during the discussion. The second part of this section was opened by F. M. LEVY (Paris) with a paper on the development of immunity in the new-born and the very young infant (pp. 31–53). This was a balanced review of the subject in which the author referred widely to the work of others and dealt fairly fully with the various factors that influence the formation of antibody and finally discussed the practical applications in developing immunization programmes. In the discussion that followed there were two prepared papers and 9 of the other participants raised specific points related to the opening paper. After answering the questions put to him the opener summed up the present position and drew attention to the many gaps in our knowledge and the need for further research.

From the report it would appear that much the greater part of the time of the conference was taken up in discussing problems related to immunization with combined prophylactics. This second session was opened by R. SOHIER (Lyons) with a paper on basic immunization with mixed vaccines, combined prophylactics or those requiring multiple injections for the reinforcement of the response (pp. 65–95). Although the French expression *les associations vaccinales* is used to cover all these, the term was originally used by RAMON for prophylactics that were commonly given together, *e.g.* TAB vaccine plus diphtheria and tetanus toxoids were grouped together or " associated " (*associé*). The list is now greatly extended and now includes the combination of toxoid preparations with enteric, pertussis, dysentery and rickettsial vaccines. It also includes the simple combination of diphtheria and tetanus toxoids. Thus any combined prophylactic that contains one or more toxoids becomes, in the strict sense, an *associé* vaccine, whereas any combination of bacterial, rickettsial or virus vaccines is called a " mixed " vaccine. SOHIER'S longish paper, about 15,000 words, covered a wide field and although it did not offer anything strikingly new it was well documented (more than 100 references which were fully representative) and made interesting reading. Officially the discussion that followed this opening paper was very long, but included in the discussion were 11 prepared papers, some of which ran into several thousand words, much of which made very familiar reading. This is inevitable at conferences of this nature where the majority of the participants are experts in their own particular field and whose original researches have already been published elsewhere.

The third section dealing with inoculation against virus diseases was entirely devoted to immunization against poliomyelitis and a consideration of the Salk and the Sabin types of vaccines was the subject of the short opening paper by J. O'H. TOBIN (pp. 195–201). He discussed the various factors which might influence the choice of a living attenuated or a killed vaccine and concluded that in the light of present day experience and knowledge both types of vaccine had their place in immunization against poliomyelitis. In immunization programmes there might be an advantage in employing the two, if the living vaccine could be given with success to infants in the first few weeks of life then the diphtheria-tetanus-pertussis vaccine could be given before the age of 6 months, followed at regular intervals by reinoculation doses of this triple vaccine combined with the killed polio-vaccine. The other communications in this section were mainly concerned with the killed vaccines.

The fourth section deals with the duration of immunity afforded by the various immunization procedures. The opening paper by R. CRUICKSHANK (pp. 219–225) was of a general nature, but most of the later communications

were concerned with the duration of effective immunity afforded by anti-tetanus and anti-diphtheria inoculations.

The final session of the symposium was devoted to a consideration of immunization programmes. Some 25 of those attending made communications, many of which were prepared papers, but although an appendix is included in the report to show the immunization programmes of 10 countries participating in the symposium these are not always very helpful. The proceedings were closed by the president, Professor DEBRÉ, who spoke appropriately and understandingly of the business which had been transacted.

While conferences of this nature may be of value to individual participants by reason of the personal contacts made at such meetings it is rarely that new information is disclosed. To those particularly interested in the subject there is little with which they are not already familiar in this very well produced report of the business conducted at the meeting. *H. J. Bensted*

DACHY, A. Projet de calendrier de vaccinations pour la Belgique. [**Immunization Programmes in Belgium**] *Bruxelles-Méd.* 1960, May 29, v. 40, No. 22, 761–77, 1 graph. [33 refs.]

This schedule of immunization procedures proposed for Belgian children appears to be the outcome of the international conference on the subject which was held in Paris in October 1959 [see REV. D'IMMUNOLOGY, above] and is concerned with the protection of young children against diphtheria, tetanus, pertussis, smallpox and poliomyelitis; BCG vaccination has not been included in the scheme outlined. The paper is relatively short and it is not deeply concerned with the details of immunological response to the various prophylactic preparations that are available, but rather the fundamentals of immunization in childhood. Combined diphtheria-tetanus-pertussis prophylactic (3 doses with 1 month interval between the doses) is recommended to commence in the first 3 months of life, vaccination against smallpox at 6th month and 3 doses of poliomyelitis vaccine at 7, 8 and 14 months. The first booster dose of the diphtheria-tetanus-pertussis prophylactic is to be given about one year after the primary immunization and the booster dose of poliovaccine about a year and a half after the last poliomyelitis immunization.

The importance of a suitable and permanent personal record card of vaccinations for every individual who has been immunized with the various prophylactics is strongly emphasized. *H. J. Bensted*

MARPLES, Mary J., MARPLES, R. R. & MUIR, B. **Microbiological Studies in Western Samoa. I. Effects of a Yaws Control Programme on the Incidence of Superficial Skin Lesions and their Aerobic Bacterial Flora, with an Appendix on the Normal Flora of the Nose.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 155–65, 1 fig. [18 refs.]

The incidence of skin infection in the inhabitants of West Samoa was investigated after a yaws control programme in which everyone was treated with large doses of penicillin. Results were compared with results obtained in a similar study undertaken before treatment [*Trop.Dis.Bull.*, 1953, v. 50, 717; this *Bulletin*, 1956, v. 31, 695].

Examination of 368 lesions compared with 454 in 1953 showed that the incidence of yaws had dropped from 26·2% in 1953 to 1·6% in 1958, the incidence of scabies was practically unaltered and the incidence of bacterial infections was, if anything, a little higher in 1958 than in 1953.

In both surveys coagulase positive staphylococci were isolated from more than 50% of all lesions, 23·8% in the 1958 series were penicillin resistant and the majority of them phage type 71. Beta-haemolytic streptococci were isolated from 47·1% of lesions in the 1958 series compared with 32·5% in 1953.

The incidence of *C. diphtheriae* from the skin was 28·7% in 1953 and 21·5% in 1958 but it was rare in the nose in 1958 (3·8%). In a survey done in 1954 the skin incidence was 48% but in 1954 many yaws lesions were sampled and the association of *C. diphtheriae* with them was not recognized at that time. 65% of *C. diphtheriae* in the present series were toxigenic compared with 18% in the 1953 survey. In the earlier survey strains were stored for some weeks before being tested for virulence and it is suggested that some may have lost virulence during this time.

Nasal swabs were also examined from the first 20 people whose lesions were swabbed in each village. There was an overall carriage rate for coagulase positive staphylococci of 21·8%, highest in the 10–19 age-group; 41·5% of the strains were penicillin-resistant. 3·7% of all people carried *C. diphtheriae*, 44·4% of which were virulent. Beta-haemolytic streptococci were not isolated but the carriage rate of pneumococci in young children was high (21·6%). *M. Patricia Jevons*

HOSPITAL AND OTHER CROSS INFECTIONS

EICHENWALD, H. F. & SHINEFIELD, H. R. **The Problem of Staphylococcal Infection in Newborn Infants.** *J. Pediatrics.* St. Louis. 1960, May, v. 56, No. 5, 665–74. [19 refs.]

This paper deals with staphylococcal infection in the newborn and no new work is presented. The authors point out that there is no satisfactory test for virulence in the staphylococci and no test for the ability of a strain to cause an epidemic.

Since it is generally accepted that infection in the newborn is by infant-to-infant transmission in the nurseries, procedures are outlined for design and running of nurseries which would break this chain of infection. Small units (4–6 infants) are advocated, working in rotation with separate staff. The unit is cleaned and restocked on discharge of each set of babies.

The place of chemoprophylaxis in nursery epidemics is discussed and the treatment of severe staphylococcal infection in infants is outlined. Intramuscular bacitracin

s suggested which is well tolerated by infants, followed y another drug to which the organism is sensitive.

M. Patricia Jevons

URST, Valerie & GROSSMAN, M. **The Hospital Nursery as a Source of Staphylococcal Disease among Families of Newborn Infants.** *New England J. of Med.* 1960, May 12, v. 262, No. 19, 951–6, 2 figs. [21 refs.]

An attempt is made to assess the incidence of staphylo-ccal disease in the families of infants born in a hospital California 14–18 months previously during an out-reak of type 80/81 staphylococcal infection.

Histories of sepsis and some cultures were taken from of the 278 infants born in hospital during the period sepsis. 27 of them had acquired strain 80/81 or its lated strain during their stay in hospital. 12 had lesions id 15 were symptomless carriers.

The home visit showed that 41 of the infants had a story of sepsis after discharge, the majority but not l were known to have been carriers of type 80/81 on aving hospital, but only about half of the infants rrying the strain at the time of the home visit had en found to be carriers on discharge. Strains were ost frequently recovered from the throat.

Staphylococcal disease developed in 20 of the mothers, of the fathers and 20 of the infants' siblings. The mber of dispersers of the strain in the family visit assessed by consideration of the clinical histories and rrier states, and it is estimated that the strain became sseminated among 65% of the families. The authors ess that the possibility of a hospital origin of family aphylococcal infection should be borne in mind by the neral practitioner.

M. Patricia Jevons

ARTIN, W. J., NICHOLS, D. R. & HENDERSON, E. D. **The Problem of Management of Nasal Carriers of Staphylococci.** *Proc. Staff Meetings Mayo Clinic.* 1960, May 25, v. 35, No. 11, 282–92. [28 refs.]

This paper is largely a review of current (mostly nerican) opinions of the place of the staphylococcal sal carrier in the genesis of staphylococcal infection, t includes a 3-month study of the detection and treat-nt of such carriers in the Mayo Clinic.

There were 86 staphylococcal carriers in the staff of convalescent poliomyelitis unit, 35 of these were given treatment; 30 had nasal sprays of antibiotic in sesame ; 10 had nasal sprays of neomycin in saline; 4 had citracin ointment and 7 subjects had systemic anti-otics [the reason for allotting a particular carrier to a rticular group is not given]. 9 of the untreated and 10 the treated carriers had associated staphylococcal ions.

Of the 35 untreated subjects 5 lost their strain, 17 were rsistent carriers and 13 had recurrences after an initial iod of freedom. 1 of the 4 bacitracin-treated carriers s cleared. In 10 of 30 carriers treated with antibiotic sesame oil the carrier state persisted and in 16 it urred after initial clearance. 7 subjects in this group had previous staphylococcal infections. Systemic antibiotics were given to 7 subjects in full dosage for 10–21 days, in 1 the carrier state was cured, in 2 it persisted and in 4 it recurred after initial elimination. Of the 10 subjects treated with neomycin in saline none became permanently negative. [Apparently none of the carriers in this series from whom the initial strain was eliminated subsequently became carriers of strains of different phage type.]

M. Patricia Jevons

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

PROC. ROY. SOC. MED. 1960, Apr., v. 53, No. 4, 253–60 (Sect. Epidem. & Preventive Med. 11–18). [21 refs.] **Symposium on Carriers of Penicillin-Resistant Staphylococci Outside Hospital** [GALBRAITH, N. S.; MCDONALD, J. C., MILLER, D. L., JEVONS, M. Patricia & WILLIAMS, R. E. O.; RYCROFT, J. A. & WILLIAMS, R. E. O.].

These 3 communications all report studies of the distribution of staphylococci which point to hospitals as the source of many pathogenic and antibiotic-resistant strains.

Galbraith studied 120 patients in general practice with boils and other staphylococcal infections. 12 (10%) had been hospital in-patients during the previous 6 months, as had 6% of their 371 household contacts: the percentage of the whole population of the country in hospital during 6 months is 3·5. The frequency of resistance to penicillin and tetracycline was greatest in staphylococci from patients who had been in hospital, less in those who had only visited hospitals, and least in those with no hospital contacts. The frequency of resistance varied little according to whether there had been previous penicillin therapy. Particulars are also given of the nasal carrier state in patients and their contacts, the strains being phage typed: in 20% of penicillin-resistant infections, but in only 5% of penicillin-sensitive, the same type was found in the contacts.

McDonald, *et al,* examined nasal swabs from 2,483 new recruits to the Royal Air Force, at the same time obtaining information about their immediate past history and certain home conditions. From 33 to 49% in different groups were nasal carriers of staphylococci. The proportion of these strains resistant to penicillin was 25% in men from homes containing a baby born in hospital, 17% when there was a baby born at home, 24% in those who had been in-patients in a hospital during the previous 9 months, 23% in those who had had a septic lesion during that time; among 1,726 men with none of these characteristics the proportion was 12%. Information is also given about the frequency of certain epidemic phage types, and carrier rates from men in different geographical areas, and in men from town and country: penicillin-resistant strains were commoner in those from rural areas.

Rycroft and Williams report the result of examining throat and nasal swabs from about 1,000 children aged 0 to 5. The carrier-rate in children born at home, 42% in the youngest age-group, fell to 21% at 2–3 years and rose again to 51% at 4–5. The frequency of penicillin-resistance in staphylococci from babies born in hospital—33% in the youngest age-group—fell almost uninterruptedly thereafter: that in babies born at home varied only between 5 and 10% throughout the period. The frequency of penicillin resistance was also higher in staphylococci from babies with a history of sepsis. Information is also given about the carrier state in child home contacts and about the distribution of different phage types among the strains isolated. *L. P. Garrod*

CHATTAS, A., RAMACCIOTTI, F., LIONETTO, M., RUDMAN, S., DE MEERSOHN, E. K. & CENTENO, R. **Staphylococcal Infections in Children. Results obtained with Different Antibiotics.** *Antibiotic Med.* New York. 1960, May, v. 7, No. 5, 300–305, 2 figs.

A study was made of staphylococcal infections in the paediatric department of the hospital of the Córdoba Medical School in Argentina over a period of 2 years. 1960 cultures were examined from various lesions and nasal secretions, and pathogenic staphylococci were isolated from 30–45% of them.

Of the 1,550 children under 2 years old admitted to hospital 7·1% had staphylococcal infections, 63·9% of them were infected before admission. Admission was most frequent in the first 6 months of life and at about 1 year. Strains from 300 children seen in the out-patients department were examined further and their source was analysed.

Coagulase-positive strains were isolated from 30 out of 80 staff in the hospital and from 27 of 46 premature infants. Limited phage typing of 33 hospital strains disclosed strains which are considered "epidemic" strains in other parts of the world.

200 strains of *Staphylococcus aureus* were examined for sensitivity to antibiotics. Only 20 were "sensitive" or "very sensitive" to penicillin and 42 to tetracycline. 54 strains were resistant to erythromycin.

The authors state that, in infants with severe staphylococcal infections, recovery was faster when treatment was based on the results of the antibiogram, but few details are given. *M. Patricia Jevons*

MILLER, F. L., ZERBI-ORTIZ, A. & ELKINS, J. T., Jr. **Use of the Tank Respirator in Overwhelming Bacterial Pneumonia.** *New England J. of Med.* 1960, June 23, v. 262, No. 25, 1264–6, 1 fig.

A man aged 37 suffering from severe staphylococcal pneumonia, with massive bilateral consolidation confirmed by X-ray, failed to respond to large doses of chloramphenicol, erythromycin and ristocetin, to digitalization and tracheotomy and bronchoscopy. He became deeply comatose with rapid shallow ineffective respirations. Arterial oxygenation, while he was receiving 6 litres of oxygen tracheally per minute, was 85 to 87·5%. He was then placed in an Emerson tank respirator. Arteri oxygenation rose promptly to 93·2%. The patient sensorium cleared rapidly. He continued to have 1 or inadequate respiratory efforts between the cycles of t respirator, set at 18 per minute. No attempt was ma to block these efforts and as the patient's conditi improved they became less frequent and disappeared aft 48 hours. The patient made a complete recovery a returned to full military duty. *A. B. Christie*

FERENCZ, Charlotte, MARKOWITZ, M. & BUNIM, J. **The Effect of Large Doses of Prednisone on Acu Rheumatic Fever. Observations on the Treatme of Seventeen Patients with Carditis with a Tw Year Follow-Up.** *J. Dis. Children.* Chicag 1959, May, v. 97, No. 5, 561–70, 4 figs.

The authors treated 17 children with clinical eviden of acute rheumatic carditis of less than one month duration with prednisone in doses of 50 to 75 mgm. dail this dosage was maintained for 9 weeks and was th tapered off in 4 to 6 weeks. The treatment produced satisfactory result as regards fever and joint manifes tions, but the recurrence rate of rheumatic symptoms a signs after the treatment stopped was 87%. 4 of the children had rheumatic heart disease at the end of years' observation and another 2 had doubtful heart sig The use of prednisone in high doses did not therefo prevent permanent heart changes in all patients; t numbers involved and the absence of controls make a other deduction impossible. The incidence of side effe of the drug was high, all the children developing mark signs of hypercorticalism [see also this *Bulletin*, 19 v. 31, 155]. *A. B. Christie*

BACTERIAL INFECTIONS

The order in this section is:—*General, Coryn bacterium, Haemophilus, Enteric bacteria, Brucell Pasteurella, Bacillus, Anaerobes, Spirochaetes, Other*

NOAD, Margaret. **Typhoid Fever.** *Pub. Health.* 19 June, v. 73, No. 9, 332–5, 1 graph.

This article consists of concise clinical reports of cases of typhoid fever; 2 of the patients were infected a laboratory and a third probably was. Chloramphe col was the most effective drug and should be used full doses both for the primary attack and for a relap should it occur. Previous inoculation with TAB vacc may have helped to localize the infection to the blo stream in the 2 laboratory workers—their faeces ne gave positive cultures. *A. B. Christie*

GRAY, J. J. **An Outbreak of Typhoid Fever.** *M Officer.* 1960, June 24, 367–9, 3 figs.

This is an account of an explosive outbreak of typh fever which occurred in a limited area of North Ke

wards the end of 1959. There were 50 cases of which were in females and 18 in males, and the age nge was from 4 to 75 years. Some particulars of the set and course of the outbreak are given. Treatment as by chloramphenicol and there were no deaths. Vi-age typing was done in 8 cases (although *Salmonella phi* was isolated from the faeces of 17 patients and om the blood of 2), and the type reported in each as E.1.

There is a full account of the investigations which were dertaken to discover the source of the infection. These d to the conviction that it was water-borne, although solute proof was lacking. It is possible that the public ater supply, which is filtered and chlorinated, became olluted because some caravan dwellers had access to a opcock which intervened between the water main and public fountain. This fountain was out of use tem-rarily because of a defect and the caravan dwellers d discovered how to obtain water by turning on the opcock which was 8–10 inches underground. A woman no had had typhoid in 1948 was 1 of the caravan vellers. She was quite cooperative, was found to be a ecal carrier of type E.1, and consented to the removal the gall bladder, from which typhoid organisms of e same type were isolated. *M. E. Delafield*

MPORESE, F. & MARTIN WEDARD, A. L'endemia tifo-paratifica in provincia di Grosseto nél periodo 1942–1957. Considerazioni statistico-epidemiologiche. [**Endemicity of Typhoid and Para-typhoid in Grosseto Province, 1942–57; Statistical Epidemiological Considerations**] *Igiene e San. Pubblica.* Rome. 1960, Mar.–Apr., v. 16, Nos. 3/4, 159–203, 10 figs. [12 refs.] English summary.

Grosseto is one of the 10 provinces of Tuscany and s 24 communes. For the purposes of the paper, the thors, the senior of whom is the Provincial Medical ficer, divide the whole period into 2: (a) a pre-anti-otic era—1942–49; (b) the antibiotic era, 1950–57. In neral, though the authors admit that the diagnosis of ratyphoid is often missed, the curves of incidence run ore or less parallel, that for typhoid being the higher. here was a moderate peak for typhoid in 1946 and a ich higher one for paratyphoid in 1948. Over both riods the province had a greater morbidity for the ars 1946–48 than for all Italy, but deaths per 100,000 pulation were very much less until 1953 when they se above the national figure, the same obtaining for se mortality where the 1953 rise above the national e was quite sharp. 1 commune (Pitigliano) which is e only one where hygienic conditions have not im-oved (owing to certain special circumstances), shows e highest relative incidence in period (b) but the betello peninsula (about 40 km. south of Grosseto) ows a high incidence throughout. The seasonal curves the 2 periods differ, because while in (a) there are e usual 2 summer-autumn peaks, the latter being the gher, in (b) the curve is much smoother, rising from ril to a plateau in July-August; the paratyphoid figures ow much sharper peaks than do typhoid. As regards e incidence in (a) females were more often affected, but in (b) the incidence was about equal. The age-groups most affected were 5–19 for males and 5–24 for females.

In the pre-antibiotic era 54% of both types of infection were admitted to hospital, but in period (b) the figures were 41% for typoid and 32% for paratyphoid. The length of stay in hospital did not appear to be materially affected by antibiotics, for which several possible explanations are given, none of which is very convincing.

[No figures of population either for the province or for the individual communes are given, and the war must have materially affected the figures in the 1942–49 period, so the 2 periods are not really comparable. The authors put forward the effect of chloramphenicol treatment on the excretion of the organisms as a part explanation of the changed seasonal incidence in period (b). In any statistical evaluation, which this paper purports to be, it is important that the diagnostic criteria are given.]

W. K. Dunscombe

ERLIK, D. & REITER, R. **Intrahepatic Typhoid Infection as Cause of the Carrier State.** *Lancet.* 1960, June 4, 1216–18.

Cholecystectomy in typhoid carriers may fail to clear the carrier condition, and the persisting focus of infection has often been suspected to be in the biliary passages of the liver. In favour of this hypothesis the authors cite 4 cases.

The common bile duct was explored in these patients because of symptoms of obstructive jaundice and cholangitis. In all 4, the deep bile passages contained living typhoid bacilli. In 3 cases the common bile duct was drained through a T-tube, and irrigated with chloramphenicol or tetracycline solutions. *Salmonella typhi* disappeared from the bile after 1 to 3 months, and faecal cultures became negative and remained so during periods of examination up to 4 years. The fourth patient whose common bile duct was not drained, still has symptoms of cholangitis as well as a persistent carrier state.

The authors therefore recommend that whenever cholecystectomy is performed for the typhoid carrier state, the common bile duct should be drained. This is an important new finding relevant to the surgery of the typhoid carrier, whereby the prognosis may well be improved.

H. Stanley Banks

SINGH, H. N. **Chloramphenicol with Hydrocortisone as an Adjuvant in the Treatment of Enteric Fever.** *J. Indian Med. Ass.* 1960, May 16, v. 34, No. 10, 387–92, 2 figs.

The author treated 81 patients suffering from enteric fever with chloramphenicol, with or without the addition of hydrocortisone. The dose of chloramphenicol was 500 mgm. as a first dose, followed by 250 mgm. every 4 hours till temperature had remained normal for 3 to 4 days: hydrocortisone was given in doses of 25 mgm. twice daily during the febrile period. The author found that in the hydrocortisone group, temperatures came

down to normal in 3·5 days as compared with 4·2 days in the group not receiving hydrocortisone.

[It is difficult from the facts given, to judge how the 5 groups of patients were selected or to compare the effects of the treatment. Laboratory diagnosis seems to have been limited to blood cultures, not all positive, agglutination tests in patients admitted after the second week of illness, and routine examination of urine.]

A. B. Christie

McMath, W. F. T. & Hussain, K. K. **A Preliminary Clinical Trial of Humycin in Salmonellosis.** *Pub. Health.* 1959, June, v. 73, No. 9, 328–31.

Of 67 patients, suffering from enteritis due to *Salmonella typhi-murium* and treated with antibiotics other than Humycin [paromomycin, also known as Humatin], 40 were still excreting the organism after treatment. Of 38 patients treated with Humycin, only 7 continued to excrete after treatment and of 25 patients, failures after antibiotics, only 6 remained excreters after treatment with Humycin. The combination of Humycin with streptomycin was successful in all of 8 patients. When Humycin was given in a dosage of under 40 mgm. per lb. body weight there were 6 failures in 22 patients, but when given in a dosage of 40–75 mgm. per lb. per day there was only 1 failure in 8 patients. The drug is given by mouth and there appears to be almost no absorption from the intestine. Salmonellae appear not to develop resistance to the drug. The authors' assessment of cure was 6 negative stool cultures obtained over 14 days and commencing 3 days after cessation of a 5-day course. The results seem encouraging, and a more extensive trial is recommended by the authors.

A. B. Christie

Coles, H. M. T., MacNamara, B., Mutch, L., Holt, R. J. & Stewart, G. T. **Paromomycin in the Treatment of *Shigella* and *Salmonella* Infections in Children.** *Lancet.* 1960, Apr. 30, 944–6.

It has been the experience at Queen Mary's Hospital for Children, Carshalton, Surrey, that the average persistence of *Salmonella typhi-murium* in the stools of infected children is 27 days, irrespective of the form of treatment given. The disadvantages of this prolonged convalescent carrier state have led the authors to test the efficiency of a new antibiotic paromomycin, in such carriers of *Shigella* and *Salmonella* organisms. Paromomycin is bacteriostatic against a considerable range of Gram-negative organisms, including shigellae and salmonellae. It is marketed under the trade name of Humatin and is said to be non-toxic to experimental animals when given by the oral route.

The subjects of the clinical trial comprised 9 children, aged 1–14 years, suffering from dysentery due to *Shigella sonnei*, 18 children, aged 1–16 years who were symptomless carriers of the same organism, 8 children aged 7–16½ years who were convalescent carriers of *Salm. paratyphi* B and 2 children aged 10 months and 8 years who were carriers of *Salm. typhi-murium.*

As a test of cure, successive daily faecal specime were cultured, beginning 48 hours after completion o standard course of treatment. The criterion of cure w the demonstration of 4 successive negative cultures. Te for staphylococcal or fungal superinfections were a made.

The dosage employed was 80 mgm. per kgm. bo weight in 24 hours [the frequency of dosage is n stated] for 5 days. Paromomycin was administered eith in the form of a syrup containing 1 gm. in 4 ml., as powder dissolved in milk, or as 150 mgm. capsules.

Sensitivity tests by the disc method showed that strains of *Sh. sonnei* and salmonellae were sensitive the antibiotic, while tests in liquid media demonstrat that the action of the agent was practically confined bacteriostasis.

The results obtained in children infected with *sonnei* were as follows: 8 out of 9 dysenteric childr were cured by a single course (the ninth required anoth drug), 15 out of 18 asymptomatic carriers were clear by a single course, 2 required 2 courses and the l remained infected, but was ultimately cured by neomyc These results were at least as good as those obtained previous years with streptomycin plus sulphonamid neomycin and other drugs.

All 8 of the children who were convalescent carri of *Salm. paratyphi B* had been treated with chlora phenicol during their acute illness: on paromomyc treatment, 4 were cleared after 1 course, 1 required courses and 3 resisted cure by 2 courses. Of the carri of *Salm. typhi-murium*, 1 was cleared by a single cou of the antibiotic while the other remained infected, b responded to another drug.

Side effects due to the antibiotic were negligib though the powder had a disagreeable taste. No to action was noted, the leucocyte counts, haemoglob levels and urine specimens showing no abnormality. 1 child, however, diarrhoea associated with a profu growth of *Candida albicans* in the stools occurred, a the same fungus appeared in the stools of another ch who remained asymptomatic.

The authors conclude that paromomycin is a high effective therapeutic weapon against *Sh. sonnei* but less effective against salmonellae, in which type of inf tions further trials are indicated, perhaps in combinati with streptomycin.

J. H. Walters

Black, P. H., Kunz, L. J. & Swartz, M. N. **Salm nellosis—a Review of some Unusual Aspec** *New England J. of Med.* 1960, Apr. 21 & 28 May 5, v. 262, Nos. 16, 17 & 18, 811–17; 864–7 921–7. [126 refs.]

In 3 successive issues of the journal, the Harva Medical School reviews the vast subject of salmonello on the basis of 165 cases seen in Massachusetts Gene Hospital in the years 1952–58. This is an increasi disease both in the United Kingdom and in the Unit States. Its dissemination has been increased by mod methods of mass processing and distribution of natura infected foods. The review covers the bacteriology a the common clinical patterns briefly, and deals in mu

eater detail with the less common categories of sal-onella infection that have been established, or are ierging, as distinct entities. The following manifesta-ns are included: osteomyelitis (long known as a com-cation of enteric fever and now being seen as a calization of infection with *Salmonella cholerae-suis, lm. typhi-murium* and others); arteriosclerotic aneur-ms infected from a salmonella septicaemia; meningitis, rticularly in young infants; postgastrectomy enteritis, ssibly associated with the loss of protection against fection afforded by the acid secretion and normal empty-g time of the stomach; post-operative salmonellosis, ually with symptoms of gastroenteritis; and salmonel-sis after antibiotics or cortisone, or complicating other seases, particularly cancer and diabetes. Double infec-ns, such as those of Salm. Tennessee and Salm. nama have also been found, and this may be more mmon than is recognised. Unusual sources of infec-n include: dried egg yolk; contact in diverse ways th infected domestic and other animals, insects, and ds; and hospital infections, which may be derived th from intra-mural and extra-mural sources and e rise to large outbreaks.

Both in its classic form of food poisoning and in its re unusual manifestations, salmonellosis is likely to lict modern man for many years to come.

H. Stanley Banks

LLWEGER, H. & IDRISS, H. **Encephalopathy in *Salmonella* Infections.** *J. Dis. Children.* Chicago. 1960, June, v. 99, No. 6, 770–77, 1 fig. [15 refs.]

The authors, writing from the American University spital, Beirut, Lebanon, describe 5 examples of cephalopathy occurring during the course of severe ness due to salmonella infections in children. Their jects comprised 4 boys between 1 and 3 years of age, d a girl of 11 years. 3 recovered completely, 1 covered but showed mental retardation, and 1 died of ite medullary failure.

The encephalopathy began with convulsions in 2 ients, the other 3 merely became increasingly drowsy. ma developed in all 5, and became sufficiently deep abolish the swallowing reflex in all. Abnormal muscle ne, varying from slight spasticity to decerebrate rigidity, s observed in every patient, but was very variable in gree and duration. Cerebral atrophy was demonstrated bsequently in the patient who was retarded on overy; air encephalography in his case showed ven-ular dilatation and increased air in the subarachnoid ce over the hemispheres.

Abnormally low levels of blood electrolytes were monstrated in 4 out of the 5 patients, though their portionate reduction varied from patient to patient. e cause of these biochemical changes is obscure, but authors postulate a neurogenic mechanism. Hyper-ic intravenous infusions of the appropriate electrolytes required to correct the deficiencies.

No electroencephalographic studies were made. The hors conclude that the encephalopathy of salmonella ections is due to the action of a bacterial endotoxin. It does not appear to be prevented by treatment with chloramphenicol. *J. H. Walters*

DIOŞI, P., SIMIONESCU, A., HENTIU, Valeria, LAZĂR, Lorica, SOIU, I., COMPANET, V. & RUSU, G. Epidemie hidrică de dizenterie în Tara Bîrsei, dată de *Shigella boydi.* [**A Water-borne Epidemic of Dysentery in the Tara Bîrsei caused by *Shigella boydii*** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Jan.–Feb., v. 5, No. 1, 55–8, 1 fig. [19 refs.] English summary (9 lines).

During the influenza epidemic in Rumania in 1959 an epidemic of dysentery occurred in Tara Bîrsei which was caused by *Shigella boydii* type VI, an organism which had not been encountered in Rumania previously. The epidemic occurred in March, 1959, and 56 persons were affected; the outbreak was explosive, with 89% of the cases occurring in the first 7 days. The affected persons had used water from the same wells, which had been contaminated with ground water as the result of a sudden thaw. The water was regarded as the source of infection, but it was not possible to isolate the causative organism from it as disinfection measures had been carried out. 29 patients had suffered from influenza 7–30 days previously, and this was considered to be a factor favouring the development of dysentery. *D. J. Bauer*

KRÖGER, E., STENGER, K., ØRSKOV, F. & NICOLLE, P. Dyspepsiehäufungen durch zwei verschiedene Sero- und Lysotypen der gleichen Coli-Serogruppe [O55:K59(B5):..]. [**Frequency of Dyspepsia caused by Two Different Sero- and Lysotypes of the same Serological Groups of *E. coli*/ O 55:K 59 (B 5): . . .**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 3, 343–53. [21 refs.]

The English summary appended to the paper is as follows:—

"A survey is given—in connection with the question of hospital dyspepsia—on recurrent dyspepsia of Coli types (DC), occurring in the Children's Hospital of the University of Göttingen.

"Part of the isolated types occurred one after the other, the others occurred simultaneously up to four types. The simultaneous accumulation of several types was also observed. Occasional testing of the flies revealed always the presence of the DC-type dominant in the hospital and also in the patients. The necessity of DC-typing within the serological Coli-O-groups (serological, biological and Lyso-types) is emphasized; otherwise one cannot distinguish between pathogenic and nonpathogenic strains, and mixed infections (2 or 3 simultaneously occurring infection chains) cannot be recognized. Two mixed infections which occurred in the Children's Hospital with types belonging to the same O-groups, are described: Biotype O 55; K 59 (B 5): [H 6] mixed with serotype O 55: K 59 (B 5): H 2 and serotype H 6 (lysotype Béthune) mixed with serotype H 4 (lysotype Weiler-Finlande)."

DOXIADIS, S. A., PAVLATOU, M. & CHRYSSOSTOMIDOU, O. *Bacillus faecalis alcaligenes* **septicemia in the Newborn.** *J. Pediatrics.* St. Louis. 1960, May, v. 56, No. 5, 648–54, 1 fig. [11 refs.]

From time to time since 1917 isolated reports have appeared on a few cases of *Bact. alkaligenes* septicaemia in infants or adults, but here is a report from the State and University Hospital "Alexandra," Athens, of no less than 33 cases seen in newborn infants during the period 1956–59. Half of these infants were premature, and the condition of 18 was unsatisfactory at birth. Of the remaining 15, 2 were found at autopsy to have subarachnoid haemorrhage, and 1 a severe congenital heart lesion. The other 12 were apparently healthy at birth, but within a day or two showed listlessness, refusal to take feeds, or cyanotic attacks, apnoea, or convulsions, or the appearance of large erythematous patches on the skin. These signs led to the finding of *Bact. alkaligenes* septicaemia.

Of the 33 babies 20 died; death occurred 12 hours to 11 days after the appearance of the characteristic red patches on the skin—well demarcated areas of redness of at least 4 cm. in diameter, of changing shape, increasing in size for a day or two and then beginning to fade. They were distributed mainly on the face, neck, abdomen, groins and thighs. The temperature was significantly elevated only in 4 cases, and only 2 of the babies had diarrhoea. A few developed meningitis. Specific treatment was ineffective, since all isolated strains of the organism were resistant to sulphonamides and to all antibiotics tested. Antibiotics, mainly chloramphenicol, were in fact used, but without apparent effect.

Stress is laid on the diagnostic value of the patchy erythematous skin lesions, although they have been found in septicaemia associated with other coliform bacilli. They are considered to be a non-specific vasomotor phenomenon. *H. Stanley Banks*

SADLER, W. W. **Present Evidence on the Role of Meat in the Epidemiology of Human Brucellosis.** *Amer. J. Pub. Health.* 1960, Apr., v. 50, No. 4, 504–14. [28 refs.]

The author has collected evidence to show that at least 1·25% of cattle carcasses and 1·15–3·5% of swine carcasses that have been refrigerated for 18 hours or more after slaughter are contaminated with organisms belonging to one of the three types of *Brucella.* Thus not only are those specifically engaged in the meat trade exposed to the risk of infection with these organisms but also those concerned in the handling of meat and meat products for the preparation of food dishes. The occupational hazard of the slaughterhouse worker in dealing with diseased animals is well recognized and to a less extent that of the farm worker who handles the animal before slaughter when investigating frank clinical cases of human brucellosis confirmed by bacteriological methods. But the problem of the so-called sub-clinical case of infection is much more difficult to define owing to the absence, in so many cases, of reliable diagnostic evidence of infection. While there can be little doubt that the reported incidence of human brucellosis is not a true index of the actual incidence, it is at present possible to give any reliable indication what this index *H. J. Benstec*

MOHR, W. Der Milzbrand in Deutschland im La der letzten zehn Jahre unter Berücksichtigung im Hamburger Tropenkrankenhaus beobachte Fälle. [**Anthrax in Germany during the last Years**] Reprinted from *Landarzt.* 1960, Jan. v. 36, No. 1, 9–11.

Anthrax is nowadays an uncommon infection in G many although it is widespread in certain countries Europe such as Yugoslavia. In Germany it occurs o in those who in the course of their occupation come i contact with imported hides and hair, in agricultu workers, slaughterers and veterinarians. The chief sou of infection is from imported animal products and i notable that in the war and post-war years 1940– during which no hides were imported, not a single c of anthrax came to light.

In the period 1949–1957 a total of 77 cases w notified and of these 8 were fatal. Of these cases were in patients who were treated at the Tropical Instit in Hamburg. All of these were cases of skin anth and none was fatal. In the treatment adopted the of serum has been entirely discarded but as soon specimens have been taken for laboratory examinati penicillin (400,000 to 1,000,000 units) and a bro spectrum antibiotic (achromycin 1–2 gm. or oxyte cycline) are administered. Supportive measures needed in severe cases and dehydrocortisone is of va in those with considerable oedema.

The importance of early diagnosis is stressed and differential diagnosis is shortly described. It is a stated that surgical treatment in anthrax infections definitely contra-indicated. *M. E. Delafiel*

BROWN, A., MOHAMED, S. D., MONTGOMERY, R. ARMITAGE, P., LAURENCE, D. R. *et al.* **Value o Large Dose of Antitoxin in Clinical Tetan** *Lancet.* 1960, July 30, 227–30, 1 fig. [12 refs.]

This is a record to establish by a controlled t whether tetanus antitoxin does in fact affect morta from the disease [this *Bulletin,* 1958, v. 33, 339; 19 v. 34, 126]. Patients were treated in Ibadan, Nige and Jamaica, while the trial was designed and analy in London. All patients received the same basic tr ment as regards sedation, antibiotics and nursing surgical procedures: the only difference was the admi tration of antitoxin to one group and its omission fr the other. The dose was 200,000 units for patients o 10 and 100,000 units for patients under 10: neonates w not included. The method of sequential analysis used so that if it became apparent during the trial t antitoxin was beneficial the trial could be stopped antitoxin given to all. This in fact happened after patients had been treated. The mortality rate was 4 among patients receiving 200,000 units of antitoxin 76% among the others, the probability of this ari by chance being less than 1 in 20. [Factors such

everity of illness, incubation period and the like are aken into account. The article can be judged fully only y studying the full text.] *A. B. Christie*

STEVENSON, J. & LEVY, I. A. **The Treatment of Tetanus: a Report of Five Cases with reference to the Use of Promazine.** *Scottish Med. J.* Glasgow. 1960, May, v. 5, No. 5, 219–23. [10 refs.]

This is a report of the treatment of 5 patients with tanus without resort to curarization. The authors ound thiopentone useful as an anaesthetic while carry- g out tracheotomy or other measures likely to disturb e patient, but dangerous to use over a long period ecause of respiratory depression. Promazine seemed to e a useful drug for control of spasms, up to 1,000 mgm. er day being given to an adult without any sign of xicity. *A. B. Christie*

BENJAMIN, M. K. **Chlorpromazine in the Management of Tetanus: Report of a Case.** *Med. J. Australia.* 1960, June 18, v. 1, No. 25, 975–6.

A woman suffering from moderately severe tetanus as treated by tracheotomy and continuous intravenous dministration of chlorpromazine in doses of 200 mgm. ily. The patient was adequately controlled on this sage and could indicate the onset of any distress to r attendants. Severe spasms, caused by tracheal toilet otherwise, could be controlled by an additional injec- n of 50 mgm. chlorpromazine into the intravenous livery tube. *A. B. Christie*

BÜRKI, F. Orientierende Untersuchung von Tierseren auf Antikörper gegen Leptospiren mittels Mischantigenen in der Komplementbindungsreaktion. I. Mitteilung. Ausarbeitung der Technik. [**Exploratory Investigation of Animal Sera by the Method of Complement Fixation for Antibodies to Leptospires with Mixed Antigens. I. Description of Technique**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Apr., v. 119, No. 4, 320–32, 3 figs. [16 refs.] II. Mitteilung. Ergebnisse im Vergleich zur Agglutination-Lysis-Reaktion. [**II. Comparison of Complement-Fixation and Agglutination-Lysis Results**] *Ibid.*, 333–43. [20 refs.]

The general purpose of this investigation was to devise method for detecting evidence of leptospire infection herds and flocks of domestic animals which would be s time consuming than the observation of agglutination d lysis of living cultures. Antigens were prepared with e three leptospires commonly causing disease in the vine species—*L. pomona. L. sejroe* and *L. grippo- phosa.* 2- to 4-week cultures at 27°C. in Korthof's edium were immersed in boiling water in screw-capped ttles for 20 minutes after enough concentrated salt lution to make them isotonic with blood was added. These antigens were found to give satisfactory comple- ent-fixation when used with antisera from rabbits hich had been injected. Cross-reactions were obtained th strong antisera but prozone phenomena which occurred with single antigens were eliminated when mixed antigens were used, and a small range of dilutions of antiserum was therefore sufficient. The heated mixed antigens could be preserved for many months in the refrigerator without loss of titre.

II. The combinations of leptospiral strains should be adapted to the variety of animal under investigation. The mixed antigens described above were tried out with 70 equine and 322 bovine sera which were all tested independently for agglutination-lysis of live cultures.

The correspondence was reasonably good, the general pattern being that the complement-fixation reactions were obtained only with more concentrated sera and disappeared more readily in the later and more chronic stages of infection.

The general conclusion is drawn that complement-fixation reactions with appropriate mixed antigens will pick up recent and active cases of leptospiral infection in a herd. *J. W. McLeod*

POPP, L. Die Epidemiologie des Feldfiebers im niedersächsischen Gebirgsvorland. [**The Epidemiology of *Leptospira grippo-typhosa* Infection in Lower Saxony**] *Arch. f. Hyg. u. Bakt.* 1960, July, v. 144, No. 5, 345–74, 6 figs. [24 refs.]

Infections by *Leptospira grippo-typhosa* known under various names—*Feldfieber,* swamp fever, field fever and others—have been reported to occur in both endemic and epidemic form but there are points in the epidemiology which are obscure. In this paper the author describes and discusses this epidemiology in the light of his own experience of the infection in Lower Saxony in the period 1949–59. In this period there were 3 epidemics among men and women engaged to gather field pea crops—281 reported cases of the infection in 1949, 116 in 1952 and 499 in 1955. There is much detailed information on the causative organism, the morbidity of the infection, its geographical distribution, age and sex incidence and mode of infection. The seasonal distribution and the weather conditions in the epidemic years receive detailed analysis. The part played by animals as vectors or reservoirs of the infection is also considered at length. The conclusions reached by the author are "that both the field mouse (Microtus arvalis) and water do act as vectors and are responsible for the occurrence of the epidemics with regard to time. With regard to the geographical distribution the field hamster (Cricetus cricetus) has been assumed as the 'primary' reservoir of leptospirae".

M. E. Delafield

PARNAS, J., LAZUGA, K., DABROWSKI, T. & KOS'LAK, A. Étiologie de la leptospirose en Pologne et vaccinations humaines. [**Aetiology of Leptospirosis in Poland; Immunization of Man**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 145–67, 2 graphs. [18 refs.]

This paper summarizes the findings, relevant to leptospirosis, of a group of workers representing many departments in the State Institute of Rural Occupational Medicine and Rural Hygiene at Lublin, Poland. This

group made yearly expeditions, from 1955 to 1958 inclusive, to an area east of Lublin, and confined by the rivers Bug, Solokija, Krzna, and Wieprz, where leptospirosis was known to have been endemic for many years.

In 1955 leptospirosis occurred as an epidemic of marsh fever and serological tests gave positive results in 321 out of 468 patients examined. The predominant serogroups were *L. grippotyphosa* (220 cases), *L. sejroe* (55) and *L. saxkoebing* (13); and these results accorded with the strains isolated—*L. grippotyphosa* (35), *L. sejroe* (8), and one not identified.

A survey was made of 3,497 small mammals representative of 17 genera. About 10% were found to be serologically positive [criterion not stated] with agglutination-lysis tests, in which 17 serotypes were used, as follows:—*L. grippotyphosa*, 221 animals; *L. sejroe*, 51; *L. bovis*, 23; *L. canicola*, 21; *L. australis B*, 18; *L. pomona*, 17; *L. saxkoebing*, 11; *L. sorex* [= *poi*] 8; *L. icterohaemorrhagiae AB*, 6; *L. australis A*, 6; *L. autumnalis*, 5; *L. hebdomadis*, 5; *L. poi*, 4; *L. mitis*, 3; *L. bataviae*, 2; *L. schüffneri*, 1; *L. ballum*, nil. From these animals 75 strains of leptospira were isolated: *L. grippotyphosa*, 39; *L. sejroe*, 14; *L. sorex*, 6; *L. australis A*, 4; *L. icterohaemorrhagiae*, 3; *L. bataviae*, 2; *L. saxkoebing*, 1; and unidentified, 6. [There are a few minor discrepancies between the figures given in the authors' summaries and those in the detailed results.] Of the animals studied, the following were the most important (number examined—number seropositive—number yielding isolates): *Microtus arvalis*, 1160—175—26; *Mus musculus*, 962—62—18; *Microtus ratticeps*, 287—40—8; *Arvicola terrestris*, 212—33—6; *Sorex araneus*, 110—6—2; *S. minutus*, 55—7—1; *Cricetus cricetus*, 142—14—3; *Erinaceus roumanicus*, 100—15—5; *Fiber zibethicus*, 92—28—1.

Domestic animals were surveyed serologically in 1955 (an epidemic year) and 1956 with markedly different results. The seropositivity rates in 1955 were: cattle, 31% (420/1,349); pigs, 17% (33/189); sheep 18% (3/17); horses, 43% (53/122); fowls, 2% (3/158). The corresponding rates for 1956 were: cattle 4% (56/1,510); pigs, 1% (2/149); sheep, 2% (2/108); horses, 14% (4/29); while 250 fowls, 193 geese, and 248 ducks were all negative.

The finding that two serotypes predominated in the human population prompted the authors to prepare a prophylactic vaccine from *L. grippotyphosa* (80%) and *L. sejroe* (20%). After satisfactory trials, the vaccine was given (subcutaneously, in two doses at intervals of 7–10 days) to a group of 1,700 persons. No ill effects were observed. This group was carefully observed and no case of leptospirosis occurred during the next season whereas the incidence was 18/1,200 among non-vaccinated people of neighbouring villages. [Details of the preparation and checks on the vaccine are given in the text.]

During the four years of these studies, the extent of the natural foci of enzootic leptospirosis was observed to diminish increasingly owing, it was considered, to the improvement works which were taking place, especially the building of a canal and the beneficial effect of land drainage which resulted.

The standards of hygiene and sanitation in the regi studied were stated to be the lowest in the whole count and the authors' conclusions and recommendatio contain nothing novel.

[It is difficult to abstract this paper adequately a those interested in animal surveys and prophylac vaccination should consult the original.] *L. H. Turner*

Alföldy, Z. Die epidemiologischen Eigenschaft der Leptospirosen in Ungarn. [**Epidemiologic Pecularities of Leptospirosis in Hungary**] *Livi Conditions & Health.* Vienna. 1960, v. 2, No. 41–9, 3 figs. [10 refs.]

In this interesting paper the author describes a discusses the present knowledge of the characteristics the epidemiology of leptospirosis with special referen to the experiences of and research on the infecti in Hungary. Although the infection is widespread different countries there are considerable differences the frequency of the different types of infecting organis and the sources from which it is transmitted to man. A important point which is stressed is that rats and oth rodents "only play a subordinate role as sources infection today, whereas the main weight has shifted infection through larger animals and the types of infe tion occurring in them". Observations point also an adaptation of the pathogenic organism to new hos

In Hungary leptospirosis appears to be widesprea Some of the evidence of this is obtained from the resu of the introduction in 1950 of compulsory notificati of non-bacterial serous meningitis which of course m result from a variety of infections, but in 760 patien notified in 1953–54 laboratory investigation showed th 208 (27%) were suffering from a leptospiral infecti A table sets out the frequency of the different types infection found in 537 cases of human leptospirosis 1949–1956—and among these the most common w *Leptospira pomona* (293), *L. canicola* (86), *L. hebd madis* (65), *and L. grippo-typhosa* (44). From 1,4 rodents examined leptospires were isolated from 70 a of these the main type was *L. grippo-tvphosa* (6 Serological examination of 615 domestic animals ga evidence that between 44% and 59% of horses, cat and pigs were infected mainly by *L. pomona* and *sejrö*. Dogs were infected mainly by *L. canicola*. Te in sheep and goats were negative.

Leptospirosis is described as a occupational disea which in Hungary occurs most frequently in the summ and mainly in the country. It occurs more in men th in women and most cases are in persons under 20 ye old. The prognosis is favourable. *M. E. Delafield*

Besseige, H. & Chambon, L. Réflexions sur les lept spiroses au Viet-Nam. [**Leptospirosis in Vi Nam**] *Bull. Soc. Path. Exot.* 1959, Jan.–Feb., v. No. 1, 64–78.

Since the first two cases of leptospirosis in Indo-Chi were reported in 1931 it has become established that t commonest serotypes in that country are *Leptosp icterohaemorrhagiae, L. canicola, L. bataviae,* and *australis A*; but there is evidence that *L. autumnalis* a *L. hebdomadis* may also be present.

Since 1951, outbreaks of leptospirosis have occurred, under ideal epidemiological circumstances, among personnel engaged in military operations. During the period of hostilities physicians became alert to the possibility of a leptospiral cause in febrile illnesses and it became obvious that the concept "leptospirosis = cterus" was no longer tenable: anicteric cases were much more common. With the advent of more peaceful imes the incidence of leptospirosis declined as a result of several factors: European and North African troops were withdrawn; the case rate among Vietnamese '37/547) was always very much lower than in other aces; and leptospirosis tended to become overlooked in he differential diagnosis of fevers.

The authors studied 25 patients with anicteric leptospirosis The diagnosis was based on rises in serological itres (agglutination-lysis) since attempts to isolate eptospires from blood and urine were unsuccessful.

The authors subdivided their cases into three clinical roups under which their main findings, including linico-pathological data, are tabulated. The first group 17 cases), of the vague "influenzal" type so common in he tropics, is that in which influenza, dengue, malaria, almonellosis and typhus are usually first considered as ossible causes. The second group (3 cases), charaterized y an enlarged liver which is tender to percussion, is ommonly assumed to be due to amoebiasis. The third roup (5 cases) consists of patients who present with one r more neurological symptoms (*e.g.*, paresis, sensory hanges, hemiplegia, epileptiform episodes, meningoncephalitis, retention of urine and faeces, etc.). The ncidence of the main findings, and of the (presumed) esponsible leptospires, is summarized below:—

Main findings	Totals	Clinical groups		
		I	II	III
Meningeal signs	15	8	3	4
Blood urea, 50 mgm. % or higher	16	11	0	5
Albuminuria	19	12	3	4
Leucocytes (per c.mm.)				
10,000 or more	15	10	3	2
5,000 or less	2	2	0	0
Polymorphs, 70% or more	19	14	2	3
Raised ESR	21	13	3	5
Muscle pain	15	10	1	4
L. bataviae	11	9	1	1
L. canicola	6	4	1	1
L. icterohaemorrhagiae	6	3	1	2
L. australis	2	1	0	1

In conclusion, the authors advocate serological tests r leptospirosis as a routine in all cases of fever curring in countries where the infection is endemic. [As might be expected, many of the authors' findings, periences, and views accord with those published in cent years from Malaya, this *Bulletin*, 1957, v. 32, 663, 4; 1960, v. 35, 892.] *L. H. Turner*

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VIRUS INFECTIONS

The order in this section is:—*General Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.*

DUGGAN, J. M. & HUNTER, W. F. **Ornithosis: Report of Five Cases.** *Med. J. Australia.* 1960, June 18, v. 1, No. 25, 976–8.

These 5 cases of psittacosis have been put on record to draw attention to the occurrence of human cases of this disease in New South Wales. There was nothing unusual in their clinical manifestations which, in fact, aroused suspicion as to their true nature. This suspicion was confirmed by the demonstration of a high or rising titre of psittacosis antibodies in the patients' sera by the complement-fixation test. Circumstantial supporting evidence was provided by the occurrence of illness or death in psittacine birds kept by the patients. With the exception of the first patient, who received chloramphenicol on the assumption that the pneumonia was bacterial, treatment was symptomatic. [What is indeed surprising is the authors' statement in 2 of the cases that antibiotics were actually withheld "in view of the provisional diagnosis of psittacosis". See also this *Bulletin* 1955, v. 30, 680, 764, bis.] *S. P. Bedson*

SEELEMANN, K. Zerebrale Komplikationen nach Pockenschutzimpfungen mit besonderer Berücksichtigung der Altersdisposition in Hamburg 1939 bis 1958. **[Cerebral Complications in Hamburg Children after Smallpox Vaccination, 1939–1958]** *Deut. med. Woch.* 1960, June 17, v. 85, No. 25, 1081–9, 1118–19. [26 refs.]

In this detailed paper the author records and analyses the experience of post-vaccinal cerebral complications in Hamburg children in the period 1939–1958. The introduction is a short description of such experience in other countries with a table which sets out the number of first vaccinations of children during the period of about 1950–58 in the different areas of the Federal Republic of Germany and the incidence of cases of post-vaccinal encephalitis which has varied in these areas from 1 case of encephalitis per 4,704 first vaccinations to 1 case in 30,162 vaccinations.

The Hamburg experience in the last 20 years is described at considerable length with particular reference to the age distribution of the vaccinated children and of those who were later diagnosed as cases of post-vaccinal encephalitis. A total of 390,104 children were immunized in this period and among these 46 developed encephalitis (14 died). In addition 97 children suffered from pyrexia with seizures and 36 had other forms of cerebral complication. Tables give some clinical particulars and the age and sex of the children who had complications.

Among the 46 children with post-vaccinal encephalitis 34 were under 4 years of age (1 in 10,805 first vaccinations under 4 years) and 12 were over 4 years old (1 in 2,226 first vaccinations). The death rate was 38% in the

under 4 year age-group as compared with 8% in the older children.

In view of the greater incidence of encephalitis after first vaccinations in the older age-group, the Hamburg health authority decided in 1955 that children who had not been vaccinated by the end of their third year of life were not to be subject to compulsory vaccination.

M. E. Delafield

EHRENGUT, W. Probleme und Ursachen der erfolglosen Pockenschutzimpfung. [**Problems and Causes of Smallpox Immunization Failures**] *Deut. med. Woch.* 1959, Nov. 27, v. 84, No. 48, 2158–60, 2183, 1 fig. [16 refs.]

A study has been made of the results of revaccination carried out after 7 days or longer in 100 children who did not respond to primary vaccination with smallpox vaccine. A normal primary response was obtained in 23 persons, including 5 who had to be revaccinated twice and 2 three times. 10 gave a latent response (delayed development of pustules at the vaccination site after unspecific local stimulation), 47 gave an accelerated pustular reaction, 4 a vesicular reaction, 4 a nodular reaction, in 8 a subcutaneous nodule was found, and 2 gave no reaction and were found to be seropositive. 2 did not report for re-vaccination. 3 cases are described in which a nodular reaction was obtained in children who were subsequently found to possess inhibiting antibody in titres of 8 or 16. The results obtained show that 65% of children who had failed to respond to primary vaccination had nevertheless developed some degree of immune response to vaccinia virus.

D. J. Bauer

BATTEN, P. J. **Present Status of Smallpox Vaccination.** A Review. *U.S. Armed Forces Med. J.* 1960, Aug., v. 11, No. 8, 876–83. [52 refs.]

SASLAW, S., KLUCK, C. & PRIOR, J. A. **Varicella Bullosa.** *J. Amer. Med. Ass.* 1960, July 16, v. 173, No. 11, 1214–17, 2 figs. [18 refs.]

Varicella bullosa is a rare manifestation of chickenpox. The view that it is a form of bullous impetigo due to complicating bacterial infection rather than to the virus of varicella is not shared by the authors of the present article. They describe 3 cases, all in children in the 6–18 month age-group in which the disease ran a typical, and benign, course. In 2 of these cases cultures from unruptured bullae were sterile. *J. Pickford Marsden*

FISH, S. A. **Maternal Death due to Disseminated Varicella.** *J. Amer. Med. Ass.* 1960, July 2, v. 173, No. 9, 978–81, 1 fig.

4 fatal cases of chickenpox occurring during pregnancy in young adults are described. In each case the clinical picture was dominated by severe pulmonary symptoms, the result of diffuse, interstitial pneumonic changes throughout the lungs, which was confirmed at autopsy in 2 of the cases. These patients also showe dissemination of the chickenpox lesions throughout man organs of the body. The first 3 patients were in th earlier stages of pregnancy. The fourth patient wa delivered of a live, premature, infant which did nc survive. *J. Pickford Marsden*

MCLEAN, D. M., WALKER, Selma J. & MCNAUGHTON G. A. **Mumps Meningoencephalitis: a Viro logical and Clinical Study.** *Canadian Med. Ass.* 1960, July 23, v. 83, No. 4, 148–51. [17 refs.]

56 patients thought to be suffering from mump meningoencephalitis were admitted between May 19 and April 1960 to the Hospital for Sick Childre Toronto. 42 samples of cerebrospinal fluid were culture for mumps virus with positive results in 17. 33 sampl of paired sera were examined and rising antihaemaggl tinin titres were found in 27 patients, in 11 of who the cerebrospinal fluid yielded mumps virus: in anoth 5 samples elevated titres were found.

[See also this *Bulletin*, 1958, v. 33, 96; 1959, v. 3 14.] *A. B. Christie*

MINISTRY OF HEALTH. **Reports on Public Health an Medical Subjects No. 100. The Influenza Epi demic in England and Wales 1957–1958.** pp. + 72, 7 figs. [36 refs.] 1960. London: H.M. St tionery Office. [4s. 6d.]

This is the third report on pandemics of influen issued by the Ministry of Health or its predecessor th Local Government Board. H. F. PARSONS reported o the three successive epidemic waves in 1889–92, and th Ministry on the pandemic of 1918–19, and now on th of 1957–58. A new variant of influenza virus A (A strain) was isolated in Peking in February 1957, but th was not generally known until 17 April. The fir outbreak on this side of the iron curtain occurred Singapore early in May, the infection having be imported by soldiers from Hong Kong. In the Unit Kingdom the first imported case was reported on 6 Jun and the first indigenous case on 28 June. Meantime 28 May strains of the new virus had been issued manufacturers for the preparation of autogenous vacci In July and August numerous outbreaks occurred bodies of troops, Jamboree scout camps, and schools the North of England.

Controlled trials of virus A2 vaccine were made various institutions, the serological results of which af 2 inoculations were known at the end of August; th indicated an order of 67% protection against Asi influenza. The strategy for dealing with a threat invasion by any new influenza virus, originating in distant country, thus became clear; it was necessary have warning as early as possible, rapid preparation quantity of the appropriate vaccine, immunization priority groups and then of the whole population of t country, provided that the disease had not by that ti become widespread in that country.

In England and Wales the spread of the epidemic 1957 to reach a peak on about 15 October was too ra

for the vaccine to be made generally available. At least 7½ million persons suffered some incapacity during the course of the epidemic. Although the fatality rate was low (estimated variously at 13 to 35 per 10,000) many thousands of deaths were caused through Asian influenza. The most serious complication was staphylococcal pneumonia, the case fatality of which was 28% in one mixed series of 155 cases, compared with 12% in a similar series of cases of non-staphylococcal pneumonia. In a small proportion of cases Asian influenza took a rapid, fulminating, and often fatal course; in one series of such cases the fatality rate was 58%, many but not all of these being associated with staphylococcal superinfection. Details are given of the control and management of the outbreak, and of medical and nursing aspects in certain groups, in Air Force personnel, schools, hospitals, the insured population, general medical practices, and among afflicted doctors and nurses themselves. Comprehensive statistical tables setting out many of these details are shown in an Appendix. *H. Stanley Banks*

MANGELSDORFF, A. F. & KRIEDT, P. H. **Influenza Vaccination, Reaction Rates, and Absentee Experience.** *Arch. Indust. Health.* Chicago. 1959, July, v. 20, No. 1, 28–35, 3 figs.

Before the 1957–1958 influenza pandemic, vaccination with a virus containing the Asian strain was offered in August 1957 to all employees of the Prudential Assurance Company of America. The vaccination programme began in September. A card was sent to all employees, with questions about a previous history of allergy, sensitivity to egg products or administration of other influenza vaccine. Return of the completed cards was taken to indicate willingness to co-operate. Any positive history of allergy was medically investigated. Those volunteers finally passed as suitable were inoculated, and a questionnaire about adverse reactions was sent to each such volunteer for completion 4 days after inoculation. 89·7% of these questionnaires were completed and returned. [The response rate to the initial approach by card is not stated.]

The reactions to the inoculation consisted of pain, swelling, redness, fever, aching and headache. Nausea occurred in 23·2% of women and 6·7% of men, and vomiting in 3·4% of women and 1% of men. In 51% of those who vomited, this was repeated. No very severe reactions were reported, and any ill effects subsided within 24 hours. Reactions were more numerous in women than in men, and diminished with the age of the subject.

The effectiveness of the vaccine was estimated by the percentage increase in sickness absence from upper respiratory causes among all employees in 1957 compared month by month with 1956. Two companies of similar standing were studied as controls. In one company the vaccine was administered in October 1957: in the other, no vaccine was administered. In September this index differed very little between the three companies. In October the company giving the vaccine early (the Prudential) showed a 65% increase in 1957 over 1956. The company giving the vaccine late showed a 98% increase, and that giving no vaccine a 102% increase. It is calculated that, excluding disability due to vaccination reactions, the Prudential employees were able to avoid 1,600 days of absence by means of inoculation.

[Disability due to the effects of the inoculation, however, was not negligible. 6% of women volunteers and 2·3% of men volunteers were reported as absent from these effects. There were 16,000 volunteers. Assuming equal numbers of men and women, and an average duration of absence of 1 day, 640 days of absence would have been lost from the effects of the inoculation itself.] *A. S. Fairbairn*

MILLER, D. L., MCDONALD, J. C., WILLIAMS, R. E. O. & WILSON, J. S. **A Trial of Bactericidal Vaccines for the Common Cold in the Royal Air Force.** *Lancet.* 1960, Feb. 13, 358–60.

RITCHIE in 1958 [this Bulletin, 1958, v. 33, 639] reported a controlled trial in which autogenous bacterial vaccines reduced the severity of colds and the time lost from work due to colds and upper respiratory infections in a group of factory workers. The authors conducted a trial in the Royal Air Force based on Ritchie's method, but modified to meet practical demands; the vaccines were prepared in the same way but the dosage schedule was modified.

293 volunteers (all but 12 were flying personnel) were divided into 3 groups: (a) 99 were given autogenous vaccine (a suspension in 0·5% phenol saline of the killed organisms—500 million per ml.—grown from tonsillar and buccal swabs); (b) 97 were given a pool vaccine constituted in the same way by mixing the washings from all the men in the group; and (c) 97 controls were given only phenol-saline. The three groups were treated similarly: deep-subcutaneous injections were given in the upper arm—first dose, 0·1 ml.; second dose (one week later), 0·3 ml.; third dose (2 weeks after the second), 0·5 ml.; fourth (reinforcing) dose (about 10 weeks after the third dose), also 0·5 ml.

The sickness records were analysed separately for the incidence and severity of all respiratory infections (a) during the total period of the trial, (b) for the period 3–6 weeks after inoculation, and (c) for the period of short-lived immunity—the first 2 weeks after inoculation. The total illness-rates in the three groups were about the same, but during the period 3–6 weeks after inoculation those in the autogenous vaccine group had significantly fewer illnesses than in the controls; on the other hand the sickness-rates in the autogenous vaccine group were higher than in the controls during the remainder of the trial. The vaccinated volunteers did not lose less flying-time than the controls except to a small degree in the first 2 weeks after inoculation with autogenous vaccine. Those who received autogenous vaccine showed some shortening of the stage of secondary infection of colds, mainly in the first 2 weeks after inoculation.

These results stand in contrast to those of RITCHIE; the authors suggest two reasons, *viz.* their volunteers had only 4 injections (as against 8 or more), and RAF personnel differ from factory workers in being less subject to colds generally. Such vaccines as they used seem unlikely to have any practical application to the

problem of the common cold in flying personnel, though autogenous vaccines, perhaps in greater dosage, merit further investigation among less healthy persons.

D. A. Cannon

DUNCAN, I. B. R. & SOMMERVILLE, R. G. **Poliomyelitis and Aseptic Meningitis in West Scotland—August 1958 to October 1959.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1960, Jan., v. 18, No. 1, 12–13.

This short paper provides an interesting summary of the isolation of viruses from patients suffering from poliomyelitis, aseptic meningitis and other diseases, made by the University of Glasgow Virus Laboratory at Ruchill Hospital. In 1958 (August to December) poliovirus was frequently isolated from cases of paralytic poliomyelitis (33 out of 63) and from aseptic meningitis (37 out of 133), whereas in 1959 (January to October) poliovirus isolations were rare, 1 being made from 25 paralytic cases [some of these paralytic cases have been shown to be due to Coxsackie A7, see GRIST, this *Bulletin*, 1960, v. 35, 1059] and none from 246 cases of aseptic meningitis. Viruses belonging to the enterovirus family have been isolated from many of the cases of aseptic meningitis, but at present the majority are not typed. [In fact the outbreak has been shown to be due mainly to what is probably a new member of the ECHO virus group now called Frater virus (Demonstration, 5th International Poliomyelitis Conference, Copenhagen, 1960), see also this *Bulletin*, 1958, v. 33, 732.]

A. J. Beale

SCHÄR, M. & LE GRAND, E. Epidemiologie der Poliomyelitis in der Schweiz im Jahre 1959. [**The Epidemiology of Poliomyelitis in Switzerland in 1959**] *Schweiz. med. Woch.* 1960, June 4, v. 90, No. 23, 630–2, 3 figs.

In 1959, 329 cases of poliomyelitis were notified in Switzerland, an incidence of 5 per 100,000, as compared with 2·0, 4·8 and 15·4 per 100,000 in the preceding years. The disease was non-paralytic in 64 cases (19·5%) and paralytic in 260 (79·0%); 25 cases were fatal. In about 40% of the non-paralytic cases the diagnosis could not be subsequently confirmed and the illness was considered to be due to Coxsackie or ECHO virus infection. Among 165 patients with paralytic poliomyelitis 132 (80%) had not received Salk vaccine, 3 (1·8%) had received 1 dose, 6 (3·6%) had received 2 doses and 24 (14·5%) had received 3 doses. In 1956 paralytic poliomyelitis mainly affected children aged 3–11 years, whereas in 1959 the 0–5-year age-group was mainly affected. The displacement towards the younger age-groups was ascribed to the effect of the mass immunization of school children during the preceding years.

D. J. Bauer

DEWAR, J. **Poliomyelitis in Nairnshire during 1958, with special reference to Vaccination.** *Med. Officer.* 1960, Feb. 26, v. 103, No. 9, 115–22, 1 fig. [10 refs.]

An outbreak of poliomyelitis in Nairnshire in 1958 is described in detail. 18 cases were reported, 14 of them paralytic. 7 of these patients made a virtually complete recovery but 2 died. Poliovirus type 1 was isolated from 11 of 16 patients examined including 2 of the non-paralytic cases. Virus isolation was not attempted in either of the 2 fatal cases. Virus was not isolated from either of the 2 vaccinated subjects (1 paralytic and 1 non-paralytic). A consultant who saw the vaccinated paralytic patient was uncertain whether the correct diagnosis was polioencephalitis or measles encephalitis. The protective effect of poliovaccine was assessed by comparing the incidence of notified poliomyelitis in children aged 6 months to 15 years eligible for vaccination. Thus 1 out of 1,453 vaccinated children was notified cases against 6 out of 406 non-vaccinated children.

[This is an interesting account of a well studied outbreak.]

A. J. Beale

GAVRILĂ, I. & IURAŞOG, G. Poliomielita la adulţi (aspecte imuno-epidemiologice). [**Poliomyelitis in Adults, Immuno-Epidemiological Aspects**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Jan.–Feb., v. 5, No. 1, 31–46, 4 figs. [60 refs.] English summary.

The number of patients with poliomyelitis admitted to the infectious diseases hospital in Cluj, Rumania, who were above 15 years of age has risen from 4 of 144 (3%) in 1949 to 14 of 124 (11%) in 1958. In a group of 5[illegible] adolescent and adult patients observed between 1955 and 1958, 37 (74%) lived in rural areas; 28 were aged up to 20 years, and 13 between 21 and 30 years. The gradual shift of the age incidence of poliomyelitis towards adult life noted in other countries is therefore taking place in Rumania, and it is suggested that this trend is due to an increase in incidence in rural areas and to changes in the properties of the virus.

D. J. Bauer

NUORTEVA, P. **Some Peculiarities of the Seasonal Occurrence of Poliomyelitis in Finland.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1958, v. 36, No. 4, 335–42, 4 figs. [12 refs.]

An explanation for the geographical alterations in the seasonal incidence of poliomyelitis in Finland is sought. The peak incidence in the southern coastal strip of Finland is about a month later than in more northern provinces and this late peak coincides with the area where the fly *Lucilia sericata* occurs. This fly is prominent in September when the incidence of poliomyelitis is highest and the fly is known to harbour polio virus [see, for example, MELNICK, this *Bulletin*, 1949, 24, 390]. Poliomyelitis is more common in the winter in the north than in the south of Finland. It is thought possible that the virus may be spread by flies which overwinter indoors or by cockroaches, but no new experimental evidence in support of this idea is brought forward.

A. J. Beale

RABKINA, S. A., SAZANOVA, V. D. & TSAUZNER, G. M. **Some Problems of the Epidemiology and Prophylaxis of Poliomyelitis in Cheliabinsk.** *Problems of Virology.* London. 1959, v. 4, No. 4, 57–60, 2 figs. [Translated from Russian.]

The gradual increase in incidence and severity of poliomyelitis in Cheliabinsk since 1953 is described. Also, after 1956, there was an increasing incidence in school as well as preschool children. Inactivated Russian poliovaccine was administered in 1958 in 2 doses to 73,388 people. Reactions were rare, being observed in 0·1%. During the period following vaccination there was an incidence of poliomyelitis of 13·6 per 100,000 in the vaccinated and 81·3 in the unvaccinated. It is concluded that the killed vaccine was safe and effective.
A. J. Beale

CHUMAKOVA, M. I. **The Use of the Complement-Fixation Test in Poliomyelitis.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 339–46, 3 figs. [22 refs.] [Translated from Russian.]

Crude monkey kidney tissue culture fluid infected with poliovirus giving titres in the range $10^{6.5-7.0}$ were used as antigens in complement-fixation tests. It was found that complement fixing (CF) antibodies developed slowly in the course of disease, being present in 47% of a small sample of sera collected during the first 14 days after onset and in 95% of sera collected 28 days or more after onset. A monospecific antibody response was very frequent by the complement-fixation test, about 4 times as frequent as by the neutralization test. Similarly detectable poliovirus CF antibodies were rare in normal people or those suffering from other diseases. Individuals given killed poliovaccine did not produce CF antibodies so that the CF test was particularly valuable in the diagnosis of disease in vaccinated people.
A. J. Beale

CHÄR, M. & BUSER, F. Immunisierung mit lebenden avirulenten Poliomyelitisviren. [**Immunization with Live Avirulent Poliomyelitis Virus**] *Schweiz. med. Woch.* 1960, June 4, v. 90, No. 23, 618–23, 4 figs. [23 refs.]

Immunization with live attenuated poliomyelitis vaccine was carried out in Switzerland in February 1958, and the immune response and distribution of the vaccine strains in the environment were studied. Type I vaccine (Chat strain) was given first; blood was taken for serological investigation before and 4–6 weeks after vaccination, and stool samples were taken after 10, 30, 60 and 90 days. Type III vaccine (Fox strain) was given after 4 weeks or later, and the same investigations were carried out. In families with more than 1 child stool samples were taken from the children in contact after 30 days. The results of investigations carried out on 56 persons given type I and 90 given type III vaccine are presented in tables and figures. 149 of 161 (92·4%) type I negative children developed homologous neutralizing antibody in titres of 50 to more than 1,000 after receiving type I vaccine; of 123 children originally lacking all types of antibody 58% were excreting type I virus 30 days after vaccination, 14% after 60 days, and 3% after 90 days. Contact infection was established in 19 of 75 children associating with vaccinated children in the home; 2 strains of virus which were isolated from contacts were not pathogenic when injected into 4 monkeys intrathalamically in a dose of 10^6 TCD50. In the group given type III vaccine similar results were obtained with regard to immune response and excretion of virus. Contact infection was observed in 1 instance among 12 families investigated.
D. J. Bauer

PRZESMYCKI, F., DOBROWOLSKA, Halina, OLAKOWSKI, T., STANCZYK, Regina & NARUSZEWICZ, Danuta. Szczepienia w Polsce żywą osłabioną szczepionką przeciw poliomyelitis. [**Vaccination in Poland with Live Attenuated Poliomyelitis Vaccine**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 1, 1–14. English summary.

Vaccination with the Chat strain of type 1 live attenuated poliomyelitis vaccine was carried out on 2,888 children and adolescents living in the town and surroundings of Wyskow, Poland, which was devoid of pipes, water supply and sewage as a result of war damage. The virus could be detected in the stools of 23 of 32 (72%) vaccinated children and in 5 of 30 (16·6%) persons in contact with them. In a similar investigation carried out in Warsaw the virus was recovered from the stools of 19 of 22 (86%) vaccinated children and 7 of 24 (29%) persons in contact. Among 114 persons in Wyskow having no type 1 antibody before vaccination 11 (9·6%) responded with a titre of 4, 30 (26·3%) with 4–32, 40 (35·1%) with 64–256, and 33 (29%) gave a titre of 512 or higher. Of the 84 persons who possessed type 1 antibody before vaccination 59 (70·1%) responded with a 4-fold or greater rise in titre.

5 of 6 strains of virus recovered from vaccinated persons produced no signs of infection on intracerebral and intraspinal injection in rhesus monkeys but in monkeys inoculated with the remaining strain the typical histopathological appearances of poliomyelitis infection were observed and 2 of 5 strains isolated from contacts also produced typical lesions on intraspinal injection.
D. J. Bauer

MARTIN DU PAN, R. & BUSER, F. La transmission de virus poliomyélitique chez des sujets en contact avec un enfant vacciné. [**The Transmission of Poliomyelitis Virus in Persons in Contact with a Vaccinated Infant**] *Schweiz. med. Woch.* 1960, June 4, v. 90, No. 23, 628–30.

Six infants aged 23 days to 1 year who were resident in a nursery in Geneva were vaccinated with the Chat strain of type I attenuated poliomyelitis virus. The virus was recovered from the stools of 4 infants, who were aged 5–12 months; the remaining 2, from whom the virus was not isolated, were aged 23 days and 1½ months respectively, and had no type I antibody either before or after vaccination. 5 of 8 infants aged 1–17 months who were resident in the same nursery became infected

with the vaccine virus and developed high titres of neutralizing antibody. Observations were also carried out on 54 families in Berne and Geneva in which a child had been given the same vaccine ; 16 of 84 (19%) children who were in family contact with the vaccinated children became infected with the vaccine virus. This percentage is lower than that observed in other countries, a difference which is attributed to the presence of better hygienic conditions, which do not favour the spread of the virus.

D. J. Bauer

Bürgin-Wolff, A., Berger, E. & Just, M. Bildung und Persistenz von Antikörpern gegen die Kinderlähmung nach Salk-Vaccination. Ein Beitrag zum Wert und zu den Grenzen der Schutzimpfung nach Salk. [**Formation and Persistence of Poliomyelitis Antibodies after Salk Vaccination. A Contribution to the Value and Limitations of Prophylactic Vaccination by the Salk Method**] *Schweiz. med. Woch.* 1960, June 4, v. 90, No. 23, 633–7, 3 figs. [18 refs.]

An investigation of the immune response to the injection of Salk-type poliomyelitis vaccine was carried out on 63 persons in Basle in 1957. In 116 persons investigated before vaccination type I antibody was absent in 68 (58·6%), type II in 64 (55·2%) and type III in 72 (62·1%). The vaccine was given in 3 doses with successive intervals of 4 weeks and 6 months. After each dose the number of non-immune persons decreased but did not entirely disappear, and after 3 doses titres below 40 of types I and II antibody were still found in 5–6% and of type III antibody in 16% of the 63 persons examined ; 11 persons (17·1%) still lacked antibody to at least 1 type of virus. The mean rise in titre of type I antibody was 2·76-fold, of type II 3·15-fold and of type III antibody 2·74-fold. Serological investigation carried out 1 year after the end of vaccination showed that an increase in titre of types I, II and III antibody had occurred in 21 (33·4%), 20 (31·8%) and 15 (23·9%) persons respectively, whereas a fall in the titres of the respective antibodies had occurred in 24 (38·2%), 22 (35·0%) and 17 (28·6%) persons. The fall was most marked in the 11–15 year age-group. From the rise in titre in one-third of the vaccinated persons it was concluded that poliomyelitis infection had occurred in spite of vaccination.

D. J. Bauer

Geffen, T. J. & Spicer, C. C. **Poliomyelitis in the Vaccinated. England and Wales, 1958.** *Lancet.* 1960, July 9, 87–9. [10 refs.]

The poliovaccination history of every case of poliomyelitis notified in England and Wales in 1958 was determined. Although there were 242 cases (137 paralytic and 105 non-paralytic) in vaccinated persons there was no indication of either provocation or inoculation poliomyelitis. Moreover, calculated attack rates for children 6 months to 15 years showed that good protection was afforded. The attack rates were 4·3 per 100,000 for vaccinated and 21·4 for unvaccinated children. The figures are 3·4 and 21·1 if those who had only 1 dose are classed as unvaccinated. In these calculations non-paralytic and paralytic cases are lumped together although it is noted that the ratio of paralytic to non-paralytic (2·5) is greater in unvaccinated than in vaccinated (2 or more doses 1·06). Deaths from poliomyelitis [which are more likely to be due to poliovirus than either paralytic or non-paralytic cases] were 10 times more frequent in unvaccinated than in vaccinated people.

[This paper provides valuable confirmation of the safety and efficacy of poliovaccine. The authors are careful to point out that their estimates of attack rates are subject to various errors, mainly in calculating the number in the vaccinated population when this changed from 1·4 to 6 million during the year. Unfortunately the lack of any aetiological studies and the combining of non-paralytic and paralytic cases together detract from the value of the assessment of vaccine effectiveness. It is now known that "non-paralytic poliomyelitis" is frequently due to viruses other than poliovirus, and, moreover, especially in the vaccinated, that poliovirus can by no means always be identified as the cause of paralytic cases.] *A. J. Beale*

Sirken, M. G. & Greville, T. N. E. **Bias in Poliomyelitis Rates based on Exposed-to-Risk Formulas.** *Human Biol.* 1959, Sept., v. 31, No. 3, 271–81.

The authors discuss the well known difficulty of comparing attack rates between two groups when there is continual transfer from one group to the other during the year and when the outbreak has a large seasonal peak. During 1957 there was an extensive campaign for poliomyelitis inoculation in the United States. The numbers of persons aged under 20 years at the beginning of the year who were inoculated, or had had 1 or 2 inoculations, or had received 3 or more inoculations were 31, 22 and 10 millions, and at the end of the year 18, 14, and 32 millions. About two-thirds of the cases of poliomyelitis occurred in the third quarter. The usual method of calculating the attack rate (number of cases in proportion to the average size of the population during the year) gave rates per million of 51·1 for the non-inoculated, 21·5 for persons having 1 or 2 inoculations and 8·2 for those inoculated 3 or more times, compared with 55·5, 22·8 and 7·5 by the authors' method of adjustment. The result is to raise the percentage effectiveness of the vaccine for paralytic cases from 57 to 58·9 (not 59·9 as given) for persons receiving 1 or 2 inoculations, and from 83·9 to 86·4 for those receiving 3 or more inoculations. *W. J. Martin*

Reploh, H. & Primavesi, K. A. Epidemiologische Beobachtungen über eine Häufung von Erkrankungen an Hepatitis epidemica. [**Epidemiological Investigations on an Outbreak of Infective Hepatitis**] *Arch. f. Hyg. u. Bakt.* 1960, June, v. 144, No. 4, 287–307, 11 figs. [55 refs.]

In this long paper the authors give a considerable account of epidemic hepatitis as recorded in many

countries where its incidence has increased considerably, and proceed to describe their investigations of an epidemic of the disease in the city of Minden, Westphalia.

Minden has a population of about 51,000. In the period from late summer 1958 to the end of August 1959 a total of 145 typical cases of icteric epidemic hepatitis were ascertained by official notification and investigation. In addition there were 26 cases of the disease without jaundice.

There is a very full account of the epidemiological observations and analysis of this experience. The incidence by season and by age is given. A map of the city spots the distribution of the cases. Sections of the paper contain descriptions of investigations in different areas of the city, in institutions for children, in schools and in families.

The main conclusion is that spread of the infection was usually by contact with infected persons and evidence of this was found in 98 cases (68%). The authors consider that virus carriers do exist.

There is a considerable discussion of the needful control measures. *M. E. Delafield*

Noordij, A. J. **An Epidemic of Infectious Hepatitis in the Children's Service of a Psychiatric Hospital.** *J. Dis. Children.* Chicago. 1959, May, v. 97, No. 5, 609–12, 1 fig.

This is an account of an outbreak of infectious hepatitis in the children's department of the Nebraska Psychiatric Institute, Omaha: there were 17 in-patients and 16 out-patients and a staff of 45. 7 of the in-patients, 2 of the out-patients and 9 of the 28 nursing staff developed the disease. Gamma globulin in doses of 0·02 cc. per lb. body weight was given to patients and staff after the second case occurred. The last case among the children developed 7 days after the use of gamma globulin and the last among staff 5 days after. It was given also to patients and staff of other divisions of the hospital where no cases at all developed. The author regards this as the only means of bringing an epidemic to an end and considers that "the effectiveness of gamma-globulin in controlling the epidemic strongly supports the diagnosis of infectious hepatitis". *A. B. Christie*

Achari, G., Das, M. & Sinha, C. N. **Drug Treatment of Infective Hepatitis.** *J. Indian Med. Ass.* 1960, June 16, v. 34, No. 12, 488–90. [12 refs.]

During an epidemic of infective hepatitis in 1958–9, different methods of treatment were tried at the Patna Medical School:—vitamin B12, chlortetracycline with a corticosteroid (bidecorticyl), chlortetracycline alone, and bidecorticyl alone: all four groups had as well ascorbic acid and vitamin B complex daily, as had a fifth group which acted as a control. The total number of patients treated was only 88.

The authors found that the group treated with bidecorticyl alone, 20 mgm. daily in 4 divided doses, did best: jaundice cleared in an average of 29·4 days compared with figures ranging from 33·2 to 45·3 in the other groups, and liver function tests returned to normal in 38·6 compared with 43·9 to 55·1 in the other groups. [There is nothing to indicate how the cases compared in severity or age and the figures are too small for any valid conclusion. It could be argued from the figures given that the use of vitamin B12 was very detrimental.] *A. B. Christie*

Mishchenko, N. K. & Shekhanov, M. V. [**The Importance of Farm Animals in the Foci of Tick-Borne Encephalitis in the Northern Part of the Kalinin Region**] *Med. Parasit. & Parasitic Dis.* Moscow. 1960, v. 29, No. 3, 271–4. [In Russian.]

The English summary appended to the paper is as follows:—

"In a focus of tick-borne encephalitis in the north of the Kalinin region farm animals play a very important part in the maintaining of the adults of Ixodes persulcatus. During the spring-summer period one cow provided sustenance, on the average, for 6–18 ticks in 1958 and for 3 to 7 ticks in 1959. Adult ticks are more numerous in cleared spaces overgrown with birches and alder trees, serving in spring and summer months as pasture for the cattle. On the spring grazing grounds the ticks are more abundant than on the territory with identical vegetation, but not used as pasture. The complement fixing tests with the antigen of the tick-borne encephalitis in cows, calves, sheep and goats revealed complement fixing antibodies (3·6–9·5% positives)."

Belikova, N. P. & Tatarinova, L. G. [**On the Part played by** *Haemaphysalis japonica douglasi* **in the Circulation of the Tick-Borne Encephalitis Virus in Nature**] *Med. Parasit. & Parasitic Dis.* Moscow. 1960, v. 29, No. 3, 287–8. [In Russian.]

The English summary appended to the paper is as follows:—

"There are still no virological data in the literature respective the part played by Haemaphysalis japonica douglasi in maintaining the reservoirs of tick-borne encephalitis.

"In 1958, the authors succeeded in isolating from the ticks of this species a virus strain of tick-borne encephalitis, which proved to possess a high degree of virulence. The information obtained testified to the presence in nature of virusophorous ticks Haemaphysalis japonica douglasi and points to their epidemiological importance in the Primorye territory, where this species is found to be widely spread within the belts of broad-leaved and cedar-broadleaved forests."

Streissle, G. Untersuchungen zur Übertragung des Virus der Frühsommer-Meningo-Encephalitis durch die Zecke *Ixodes hexagonus* Leach. [**The Transmission of the Spring-Summer Meningoencephalitis Virus by the Tick** *Ixodes hexagonus*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 3, 289–97, 3 figs. [23 refs.]

The English summary appended to the paper is as follows:—

"After subcutaneous injection of 10^5 to 10^6 LD_{50} (mice) of spring-summer meningo-encephalitis virus, mice aged six weeks, develop viremia that lasts for seven days. Maximal titers (10^3 to 10^4 LD_{50}—mice—) are reached 3 days post infectionem. These animals could be used as infectious sources for larvae and nymphae of Ixodes hexagonus. The virus of infected larvae and nymphae remained active after ecdysis and was transmitted by infected nymphae and imagines to healthy mice by bite."

HOAGLAND, R. J. **The Clinical Manifestations of Infectious Mononucleosis. A Report of Two Hundred Cases.** *Amer. J. Med. Sci.* 1960, July, v. 240, No. 1, 21–9, 1 fig. [13 refs.]

The author analyses the symptoms and signs in 200 cases of infectious mononucleosis, 191 of which occurred in patients aged 17 to 29. He holds that the disease is not so protean as is usually claimed and that there are 3 main clinical types—pharyngeal, typhoidal and icteric. The palatal enanthem he regards as not specific to infectious mononucleosis, but eyelid oedema, although present in only 50% of patients, is a helpful sign. [There is nothing in this article which a physician familiar with the condition will not know. The author seems not to be familiar with the pharyngeal type in which the fauces are covered with thick membrane—he states that the exudate is usually spotty, infrequently involving the whole throat. In Britain the membranous type resembling diphtheria is a common syndrome.]

A. B. Christie

EGAN, R. W. **Facial Diplegia in Infectious Mononucleosis in the Absence of Landry-Guillain-Barré Syndrome.** *New England J. of Med.* 1960, June 9, v. 262, No. 23, 1178–9.

A man aged 18 developed severe bilateral facial weakness 3 weeks after a pyrexial illness. Blood count and Paul Bunnell test showed that the patient was suffering from infectious mononucleosis. The author claims that this is only the third reported case in which facial diplegia occurred in infectious mononucleosis in the absence of more widespread neurological involvement.

A. B. Christie

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

THOMAS, C. G. A. & GIBBS, F. J. **Misleading Sputum Cartons.** *J. Clin. Path.* 1960, May, v. 13, No. 3, 261–3.

Viable counts made on 2 ml. of digest broth which had been placed in waxed paper cartons, sealed with the lid and shaken vigorously 10 times, showed that 50 cartons examined straight from the manufacturer contained, on the average, 3 organisms, but the average count of 50 cartons that had been kept in the store was 44 and the average number in 100 cartons recovered from the medical and surgical wards was 419. The flora of the cartons from the stores consisted mainly of *Streptococcus* sp., *Neisseria* sp. and *Bacillus* sp., but that of the cartons from the wards was more varied and included *Staphylococcus aureus* and *Escherichia* sp., *Proteus* sp., *Pseudomonas pyocyanea* and *Aspergillus fumigatus.*

That the contaminants were derived from the air was supported by the fact that cartons derived from a ward containing a patient with exfoliative dermatitis and known to be disseminating many staphylococci were found to be contaminated with many of these organisms. Of these contaminants the authors considered that *Staph. aureus* and *E. coli* were most likely to cause confusion in the examination of sputum, and they recommend that when these wax cartons are used, they be stored individually wrapped, in a dust-proof container or with their lids on.

S. R. M. Bushby

RAVIN, A. W. **The Origin of Bacterial Species: Genetic Recombination and Factors limiting between Bacterial Populations.** *Bact. Reviews* 1960, June, v. 24, No. 2, 201–20. [86 refs.]

ROUX, J., with the technical collaboration of A. L. ENJALBERT. La multiplication des formes L. [**The Multiplication of L Forms**] *Ann. Inst. Pasteur* 1960, Aug., v. 99, No. 2, 286–96, 1 fig. [16 refs.]

DAVERN, C. I. & MESELSON, M. **The Molecular Conservation of Ribonucleic Acid during Bacterial Growth.** *J. Molecular Biol.* London. 1960, Aug., v. 2, No. 3, 153–60, 5 figs. & 1 pl.

BILLEN, D. **Effects of Prior Alteration in Nucleic Acid and Protein Metabolism on Subsequent Macromolecular Synthesis by Irradiated Bacteria.** *J. Bacteriology.* 1960, July, v. 80, No. 1, 86–95, 8 figs. [21 refs.]

WILDFÜHR, G. **Medizinische Microbiologie, Immunologie und Epidemiologie. Vol. I.**

This book was reviewed on p. 1070.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

CLUZEL, R., VAURS, R., CLUZEL-NIGAY, M. & VERNER, M. Une nouvelle technique d'étude du pouvoir bactéricide des associations d'antibiotiques, dérivée du "transfert sur cellophane": la disposition en croix. [**A New Technique for the Study of the Bactericidal Power of Antibiotic Associations derived from "Transfer on Cellophane": Cross Disposition**] *Ann. Inst. Pasteur.* 1960, June, v. 98, No. 6, 928–32, 1 diagram & 2 figs.

These authors describe a modification of the method first described by CHABBERT [this *Bulletin*, 1958, v. 33, 158], which enables 4 combinations to be tested on one plate instead of only 1. Chabbert placed 2 antibiotic-containing strips of blotting paper at right angles on the first plate; in the present method 4 strips are placed on it in the form of a cross. Otherwise the method is the same: the strips are removed after diffusion from them, and the "drum" of Cellophane, inoculated by flooding with culture, is placed on the medium. After incubation for one day the Cellophane is transferred to a fresh plate of medium, to enable the organisms to grow, which have been inhibited but not killed. The behaviour of the combination is judged by what happens in the angle between 2 strips. Synergic and antagonistic effects are illustrated, but the only antibiotics in each of the two plates all belong to the group of macrolides. Against one strain of staphylococcus the combination erythromycin + oleandomycin was synergic: against the second strain this and two other such combinations showed antagonism. [The unusual phenomenon of antagonism between antibiotics of this group is characteristic of staphylococci possessing the "dissociated" type of resistance [GARROD, this *Bulletin*, 1957, v. 32, 1090], but synergy is more difficult to understand. Tests with pairs of unrelated antibiotics could better illustrate the possibilities of the method.] *L. P. Garrod*

GILLISSEN, G. & GILLISSEN, Ilse M. Die Resistenzbildung bei Mikroorganismen. [**The Development of Resistance in Micro-organisms**] *Ergebn. Mikrobiol. Immunitätsf.* 1960, v. 33, 128–41, 14 figs. [Numerous refs.]

This is a comprehensive but condensed review, concluding with 35 pages of references (with titles). It is divided into 4 main parts, the first dealing with the attributes of resistance, including its degree and rate of development, cross-resistance with other substances, and accompanying changes in morphology, metabolism, serological reactions and other properties. The second deals with the basis of resistance, which may depend on enzyme formation, the formation of an antagonistic substance, or failure of the drug to reach its site of action. The third and longest section first describes methods of obtaining resistant variants, either *in vivo* or *in vitro*, "single-step" and "multi-step" changes, methods of proof that resistance can depend on spontaneous mutation, and the phenomena of transformation, transduction and recombination. A short final sub-section on non-genetic changes cites examples of adaptation, but insists that the capacity for adaptation is also genetically controlled. A short final section on the reduction or prevention of resistance is chiefly concerned with the effect of drug combinations, but refers also to anti-mutagens and the Welsch phenomenon (the overgrowth of resistant variants by sensitive owing to the difference in their generation time).

Protozoa are extensively referred to as well as bacteria. In cataloguing so much work the authors have evidently been able to afford little space to express their own opinions on it. This is not often necessary, but when papers are cited by an author who pretended to have shown that all resistance is dependent on a change of intracellular *p*H it could with advantage have been added that no one has confirmed this. It is as a guide to the literature, even though this is of varying merit, that this review will be found chiefly of value.

L. P. Garrod

DVORSKÝ, K. Veränderungen in der Empfindlichkeit einiger *Salmonella*- und *Shigella*-Bakterien gegen verschiedene Antibiotica *in vitro* in den Jahren 1955 und 1958. [**Changes in the Sensitivity of some *Salmonella* and *Shigella* Bacteria to Different Antibiotics *in vitro* in 1955 and 1958**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 178, No. 3, 310–20. [25 refs.]

This paper concerns 501 strains isolated in 1955 and 497 in 1958. They include *Salmonella typhi* and *para-*

typhi B, 10 food-poisoning salmonellas, and *Shigella sonnei* and *flexneri*. Unfortunately many of their numbers are very unequal in the 2 years and 6 species are represented only in 1 year. Sensitivity was tested by applying discs freshly saturated with antibiotic solution (50 and 100 μgm. in 1955, only 100 μgm. in 1958) to heavily inoculated blood agar plates. The results are presented and analysed in a series of Tables, 2 of which are on folding pages. The antibiotic to which the highest overall percentage of strains was sensitive in 1955 was streptomycin: in 1958 it was neomycin, but this was not included in the 1955 tests. For some organisms there was an increase in the frequency of resistance to streptomycin, and for some a diminution. The most unequivocal change was an increase in the frequency of resistance to chlor- and oxy-tetracycline. A pronounced change in the opposite direction is shown as having occurred in relation to chloramphenicol, but this is discounted in the text because the drug came from different sources in the 2 years, and the 1955 supply is said to have been "less soluble" [neither supply was obtained from the firm holding the patent rights]. Much of the space in tables and text is taken up by an analysis of relationships between resistance to different antibiotics.

L. P. Garrod

ENGLISH, A. R., HUANG, H. T. & SOBIN, B. A. **6-Aminopenicillanic Acid in Urine after Oral Administration of Penicillins.** *Proc. Soc. Exper. Biol. & Med.* 1960, July, v. 104, No. 3, 405–6.

SUZUKI, K. & IWAMA, Y. **Recovery in the Presence of Chloramphenicol of *Escherichia coli* B(H) irradiated with Ultra-Violet Light.** [Correspondence.] *Nature.* 1960, July 23, v. 187, 347–8, 2 figs.

LUNDSGAARD-HANSEN, P., SENN, A., ROOS, B. & WALLER, U. **Staphylococcic Enterocolitis. Report of Six Cases with Two Fatalities after Intravenous Administration of N-(Pyrrolidinomethyl) Tetracycline.** *J. Amer. Med. Ass.* 1960, July 2, v. 173, No. 9, 1008–13, 3 figs. [17 refs.]

These authors from Berne, Switzerland, give a report of 6 cases in which acute staphylococcal enterocolitis followed the administration of N-(pyrrolidinomethyl) tetracycline (a form of tetracycline administered intravenously, known as Reverin in Germany and Syntetrin in the U.S.A.). In all the cases the antibiotic was given as cover for an operation, usually in 2 daily doses of 250 mgm. for 4 days. In the 4 patients who recovered the operations were for insertion of aortic or iliac artery prostheses, excision of carcinoma of the colon, and plastic repair of rectal prolapse. Treatment consisted of stopping previous antibiotic treatment, administering erythromycin or spiramycin, and fluid replacement. The 2 fatal cases were a man aged 35 after iliac endarterectomy and lumbar sympathectomy, and a woman aged 56 after a cholecystectomy. This patient had no diarrhoea, although the changes in the bowel at post mortem were typical, the exudate over areas of mucosal necrosis in the small intestine "containing a veritable blanket of staphylococci".

It had been supposed that because this form of tetracycline is not administered by the alimentary route, it does not affect the bowel flora [this assumption disregards the fact that tetracyclines are excreted in high concentration in the bile, thus reaching the part of the bowel, the upper small intestine, in which the lesions of staphylococcal enterocolitis are usually most extensive]. These cases show that patients given tetracycline in this form "must be watched just as closely for this complication as those receiving any other tetracycline derivative".

L. P. Garrod

HAUCK, Senta. Bakteriologische Untersuchungen über Kanamycin. [**Bacteriological Studies of Kanamycin**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 433–9. [21 refs.]

The author remarks that although kanamycin is now available in Germany, little has been published about it in German literature, most publications being Japanese or Anglo-American. His own work consisted first of determining the activity of kanamycin against a variety of bacteria: the results confirm the high sensitivity of staphylococci, the sensitivity of *Escherichia coli* and *Proteus*, and the relatively greater resistance of all kinds of streptococci and *Pseudomonas pyocyanea*. This was done by a tube dilution test in broth: sub-culture showed that the bactericidal concentration was the same as or little more than the bacteriostatic. These findings were extended to much larger numbers of strains by a disc test, the results being given simply as percentages sensitive. Strains of *Staphylococcus aureus* totalled 994, of which 99% were sensitive: the percentages of these sensitive to 9 other antibiotics are also given. Tests of cross-resistance with streptomycin and neomycin were also done, showing a fairly close but not constant relationship. Blood levels were determined in 6 or 8 subjects at intervals after an intramuscular dose of 1 gm.: the average quantities found after 1, 2, 4, 6 and 12 hours were 39·4, 30·4, 10·1, 5·1 and <3 μgm./ml. *L. P. Garrod*

DRIES, C. P. & KOCH, R. **Clinical Evaluation of Ristocetin in Children. A Preliminary Report.** *J. Dis. Children.* Chicago. 1960, June, v. 99, No. 6, 752–6. [10 refs.]

This paper from Los Angeles reports the treatment with ristocetin of 76 children, 47 of whom had staphylococcal infections. The intravenous preparation was injected intramuscularly, 1 mgm. hydrocortisone per 10 mgm. antibiotic being added to suppress local inflammatory reaction: in this it appears to have been successful and no effect on adrenal function could be detected. It is difficult to assess therapeutic results, since few details are given and no individual case histories: some of the more seriously ill patients were also given other antibiotics. A dose of 50 mgm. per kgm. daily was more successful than half this dose, but was also more

liable to cause reactions: these included leucopenia (considered an indication for stopping treatment), eosinophilia and rashes, but not thrombocytopenia. The over-all recovery rate was 87%, and the list of conditions treated includes septicaemia, endocarditis and other severe infections. *L. P. Garrod*

Dries, C. P. & Koch, R. **Ristocetin, a Laboratory and Clinical Evaluation in Children.** *J. Pediatrics.* St. Louis. 1960, Apr., v. 56, No. 4, 498–504, 4 figs. [15 refs.]

This paper is based on the same series of cases as the foregoing, but includes some other data. The most important of these are the results of assays of ristocetin in the blood of children at intervals after doses of 12·5 and 25 mgm. per kgm. by both the intravenous and the intramuscular route, there being 8 or more patients in each of these dosage groups. With the larger dose satisfactory levels were maintained for 12 hours, and it is recommended that in children this dose be given twice daily. As reported in the other paper, it was clinically more effective than the smaller dose: it also caused more reactions, particulars of which are again given. Assays of ristocetin were carried out with 12 specimens of normal cerebrospinal fluid and 1 from a patient with meningitis. No antibiotic was detected in any of them: ristocetin is therefore not recommended for the treatment of meningitis. A few particulars of individual cases are given, including complete charts of fever, laboratory findings and therapy in 3 patients, which illustrate the limitations of this antibiotic rather than its better achievements. *L. P. Garrod*

Marsh, W. S., Garretson, A. L. & Wesel, E. M. **PA 155 A, B, and X. Antibiotics Produced by a Strain of** *Streptomyces albus.* *Antibiotics & Chemotherapy.* New York. 1960, May, v. 10, No. 5, 316–20.

This paper from the laboratories of Chas. Pfizer and Company, New Jersey, records the isolation from a strain of *Streptomyces albus,* the somewhat atypical characteristics of which are given in detail, of an antibiotic having 3 components, designated A, B and X, the yields of which can be varied by changes in medium composition. Nothing is said of the action of these individual components, but a simple culture filtrate was shown to be active against *Bacillus subtilis* and *Staphylococcus aureus,* the latter including strains resistant to tetracycline, erythromycin and carbomycin. *L. P. Garrod*

Hurst, A., Stuttard, L. W. & Woodroffe, R. C. S. **Disinfectants for Use in Bar-Soaps.** *J. Hygiene.* 1960, June, v. 58, No. 2, 159–76, 5 figs. [50 refs.]

This paper from the Food Research Department of Unilever Ltd., is in 2 parts. The first reports some *in vitro* tests of the activity of 7 germicides recently introduced for inclusion in soaps. These were hexachlorophene (G11), thiobis dichlorophenol (Actamer), dichloro-*m*-xylenol (DCMX), tetramethyl thiuram disulphide (TMTD), trichlorcarbanilide (TCC), tribromosalicylanilide (TBS) and tetrachlorsalicylanilide (TCS). Simple tests of bacteriostatic action showed *Staphylococcus aureus* to be inhibited by concentrations varying from 0·1 to 2·5 p.p.m., and *Escherichia coli* by 12·5 to 50 p.p.m. A "soap inactivation coefficient" was obtained by agar diffusion tests from cylinders containing solutions with and without soap. DCMX had no activity in the presence of soap, and G11 had a coefficient of 208 (*i.e.* its activity was greatly reduced by soap) but the remainder had coefficients varying only between 2·6 and 0·32. Serum reduced the activity of all the germicides to a varying extent: dirt washed off the skin had little effect on any.

The second part reports some observations on the effect of soaps containing these substances (except DCMX) in concentrations of 0·2–2·0% on the numbers of bacteria recoverable from the skin in a hand-washing test. The authors were dissatisfied with existing methods for such a test, particularly with the erratic counts obtained, and devised a modification of their own. The results of one separate test are given in detail: this was done with a soap containing 3% of a mercuric salt (chloride in the text: iodide according to the legend in the figure showing the results) and a reduction of over 90% in the bacterial count was achieved. Use of soaps containing the 6 other germicides for 1 week appears to have failed in every case to achieve as great a reduction as this: reductions varied only beween 56 and 84%, the latter being achieved by a soap containing 0·5% TCS. Higher concentrations of this germicide were not tested. *L. P. Garrod*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

JELJASZEWICZ, J. Badania nad koagulazami gronkowcowymi. V. Obserwacje ilościowe dotyczące wytwarzania wolnej koagulazy przez szczepy gronkowców pochodzące z różnych zródeł. [**Studies on Staphylococcal Coagulases: V. Quantitative Observations concerning the Production of Free Coagulase by Staphylococcal Strains from Different Sources**] *Med. Dośw. i Mikrob.* Warsaw. 1960, v. 12, No. 1, 21–32. [16 refs.] English summary. VI. Wystepowanie różnych czynników toksycznych i biochemicznych wśród koagulazo-ujemnych i koagulazo-dodatnich szczepów gronkowców. [**VI. Some Characteristics of Coagulase-Negative and Coagulase-Positive Staphylococcal Strains**] *Ibid.*, 33–41. [39 refs.] English summary.

I. In an examination of 1199 strains of *Staphylococcus aureus* isolated from carriers in the area of Poznan, Poland, free coagulase was found in titres of 10–320 in 429 (35·8%), 640–1280 in 262 (21·9%) and 2560–5120 in 82 strains (6·8%). The corresponding figures for 414 strains isolated from children and adults suffering from staphylococcal infections were 153 (36·9%), 118 (28·5%) and 56 (13·6%) respectively. There was no relationship between the amount of free coagulase produced and the pathogenicity as judged by clinical findings.

II. 746 strains were also investigated for the presence of 17 characters of pathogenicity or other biochemical criteria, and the results are presented in tables. Pathogenicity was commonly associated with the presence of free and bound coagulase, alpha- and delta-haemolysins, leucocidin, ability to grow in serum, anaerobic fermentation of mannitol and phosphatase. *D. J. Bauer*

FAHLBERG, W. J.; MARSTON, Judith. **Coagulase Production by *Staphylococcus aureus*. I. Factors influencing Coagulase Production** [FAHLBERG & MARSTON]. *J. Infect. Dis.* 1960, Mar.–Apr., v. 106, No. 2, 111–15. [24 refs.] **II. Growth and Coagulase Production in Complex and Chemically Defined Mediums—Comparison of Chemically Defined Mediums** [MARSTON & FAHLBERG]. *Ibid.*, 116–22, 3 figs. [21 refs.]

I. The coagulase production of 3 strains of *Staphylococcus aureus* was studied. Bacto brain heart infusion (BHI) medium to which trace elements had been added, and a dialysate of the same medium, were used. Free coagulase was estimated by incubating serial dilutions of culture supernates with equal volume of 1:5 human plasma, for 6 hours at 37°C. in a water bath.

Coagulase production was constant and similar in both media. Titres ranged from 1:28 to 1:512 and the addition of lithium chloride (which inhibits bound coagulase) to the medium did not affect the titres. Production was not increased by the addition of peptone, yeast extract, bovine serum albumin or by the 4 carbohydrates and 6 polyhydric alcohols tested. A fall in the medium to *p*H 4·8 in the presence of high concentrations of fermentable carbohydrate inhibited coagulase production.

Production did not appear to be increased by aeration, the addition of CO_2 or prolonged incubation, but yields were higher when the culture was shaken during growth.

II. The 3 strains used in experiments described in the previous paper were grown in the dialysed BHI medium and 2 chemically defined media, and growth and coagulase production in each were compared.

One medium (HSVA) was a modification of that of HENDERSON and SNELL (*J. Biol. Chem.*, 1948, v. 172, 15) and the other (MS) was a modification of MERGENHAGEN's medium [this *Bulletin*, 1958, v. 33, 884]. HSVA contained a number of B-complex vitamins and some buffer salts which were lacking in MS, but MS contained L-histidine HCl, L-lysine HCl and L-glutamic acid, which were not present in HSVA.

Coagulase was detected in the lag phase and the log phase of growth but ceased in the stationary phase. Both synthetic media supported the growth of the 3 test strains, but less well than the dialysed medium. Coagulase was produced by 2 strains in MS medium with titres similar to those produced in the dialysed medium. One strain (104) produced only low titres. 3 strains grown in HSVA medium produced only small amounts and strain 104 produced no detectable coagulase.

The addition of the 3 amino acids present in MS medium only to HSVA medium stimulated coagulase production, and possible mechanisms for this are discussed. *M. Patricia Jevons*

KAPRAL, F. A. & LI, Isabel W. **Virulence and Coagulases of *Staphylococcus aureus*.** *Proc. Soc. Exper. Biol. & Med.* 1960, May, v. 104, No. 1, 151–3.

The relationship between virulence and the ability of a strain of *Staphylococcus aureus* to produce bound and soluble coagulases was investigated. A virulent strain 18Z of phage type 42B/52/80/81 was chosen for the experiments. It produced both coagulases, alpha and delta haemolysin, leucocidin, hyaluronidase and fibrinolysin. A washed suspension of organisms was irradiated to give a 1% survival and 3 mutants were isolated from the survivors; 18Z-B which produced soluble but no bound coagulase; 18Z-C which produced bound, but lacked soluble coagulase and fibrinolysin and 18Z-D which produced both types of coagulase. The 3 mutants were in other respects similar to the parent strain.

Rabbits were injected intracutaneously or intravenously with 10^8 organisms of each of the 3 mutants and the parent strain. Intracutaneously injected animals were observed for local lesions and animals injected

intravenously were sacrificed after 7–10 days and the liver and kidneys examined for staphylococci.

Results obtained were consistent. Animals given 18Z-B (lacking bound coagulase) or 18Z-C (lacking soluble coagulase) by either route produced lesions similar to the parent strain, and organisms recovered from lesions were identical in their coagulase activity with the mutant inoculated. Mutant 18Z-D which produced both types of coagulase however was avirulent although identical with the parent strain in every other property tested.

Results suggested that although there is a high correlation between coagulase production and virulence, coagulases are not essential for virulence of *Staph. aureus*.

M. Patricia Jevons

h. North, E. A. & Doery, Hazel M. **Antagonism between the Action of Staphylococcal Toxin and the Venom of Certain Snakes and Insects in Mice.** *Brit. J. Exper. Path.* 1960, June, v. 41, No. 3, 234–42. [14 refs.]

i. Doery, Hazel M. & North, E. A. **Factors involved in the Action of Venoms against Bacterial Toxins in Experimental Animals.** *Ibid.*, 243–50, 1 fig. [22 refs.]

(i) These authors at the Commonwealth Serum Laboratories, Melbourne, apparently began this study with the object of improving the production of staphylococcus antitoxin, but it developed in another direction. The original argument was as follows: staphylococcus toxin immunizes better than toxoid, but causes lesions believed to result from vasoconstriction: if an antagonist to this effect could be given at the same time which did not alter the antigenicity of the toxin, immunization might be facilitated. A snake venom with a vasodilator action was chosen and in fact a fraction of the venom of the tiger snake was found first to diminish the dermonecrotic action of the toxin in mice, and in later experiments to protect against its lethal action when the toxin was injected intravenously, but not when it was given intraperitoneally: there was also little effect on the results of subcutaneous toxin injection. The active substance in the venom was heat-stable, and treatment with formalin increased its activity. This "toxoid" venom somewhat increased survival after intraperitoneal inoculation with staphylococcus culture.

(ii) The second paper describes an endeavour to elucidate this effect, proceeding from the hypothesis that the active substance in venom is phosphatidase A: the activity of different samples varied with their content of this enzyme, and that of the black snake, which has a high content, was thenceforth used. The products of the action of phosphatidase A on phosphatides in the body are lysophosphatides and long-chain fatty acids: the protective action of some of these against the lethal effects of staphylococcus toxin was therefore examined, and both lysolecithins and oleic and other unsaturated fatty acids were found to have such an action. It is therefore suggested that phosphatidase A and other enzymes may "take part in a natural defence mechanism against bacterial toxins".

L. P. Garrod

Rogers, D. E. & Melly, Marian A. **Further Observations on the Behavior of Staphylococci within Human Leukocytes.** *J. Exper. Med.* 1960, Apr. 1, v. 111, No. 4, 533–58, 14 figs. [26 refs.]

In view of the work of Cohn and Morse [this *Bulletin*, 1960, v. 35, 389] on interactions between staphylococci and rabbit polymorphonuclear leucocytes, the authors extended the original work of Rogers and Tompsett [this *Bulletin*, 1952, v. 27, 691] on the survival of staphylococci in human leucocytes.

Two strains of *Staphylococcus*, one coagulase-positive, the other coagulase-negative, obtained from Cohn and Morse, were added to suspensions of human leucocytes (obtained by dextran sedimentation) in siliconed tubes which were agitated continuously in an incubator maintained at 37°C. for varying periods.

It was found that a specific serum factor was required for rapid phagocytosis of pathogenic staphylococci when the concentrations of the latter were low. A factor promoting phagocytosis was found in all the 8 human sera used; in contrast the sera of 28 out of 30 normal rabbits did not promote phagocytosis. The phagocytosis-promoting factor was almost completely removed by prior absorption of test sera with the homologous strain; it was incompletely removed by absorption with heterologous strains of pathogenic staphylococci and was not significantly reduced by absorption with coagulase-negative staphylococci or unrelated micro-organisms. It would appear that this phagocytosis-promoting factor is a thermostable opsonin.

Once ingestion was accomplished, coagulase-positive staphylococci consistently survived in significant numbers within the cytoplasm of human granulocytes. Coagulase-negative staphylococci appeared to be destroyed within the leucocyte and could not be recultured from the cytoplasm after 3 to 4 hours of intracellular residence.

D. A. Cannon

Baum, H. & Crowley, N. **Starch-Like Polysaccharide of** *Streptococcus pyogenes*. [Correspondence.] *Nature*. 1960, July 30, v. 187, 413.

Kantor, F. S. & Cole, R. M. **Preparation and Antigenicity of M Protein released from Group A, Type 1 Streptococcal Cell Walls by Phage-Associated Lysin.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 77–96, 4 figs. [25 refs.]

Smith, E. E. B., Mills, G. T., Bernheimer, Harriet P. & Austrian, R. **The Synthesis of Type III Pneumococcal Capsular Polysaccharide from Uridine Nucleotides by a Cell-Free Extract of** *Diplococcus pneumoniae* **Type III.** *J. Biol. Chem.* 1960, July, v. 235, No. 7, 1876–80, 1 fig. [31 refs.]

Bird, G. W. G. **Anti-Pneumococcus Type XIV Activity of Precipitins from** *Ricinus communis* **Seeds.** [Correspondence.] *Nature*. 1960, July 30, v. 187, 415–16.

AUHAGEN, H. Bedeutung und Gewinnung von Einzell-Kulturen bei Mycobakterium tuberculosis. [**Significance and Technique of Single Cell Culture with** *Mycobacterium tuberculosis*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 2, 192–207, 22 figs. on 3 pls. [32 refs.]

The methods of obtaining highly dispersed cultures of *Myco. tuberculosis* and the conditions in which growth can be obtained from solitary bacteria isolated with the Zeiss micromanipulator are discussed. The stages in the development of a microcolony from a single bacterium have been filmed and illustrations from these are included. *J. W. McLeod*

FOURNIER, F. Étude de *Mycobacterium tuberculosis* par diffraction de rayons X. [**Study of** *Mycobacterium tuberculosis* **by X-ray Diffraction**] *Rev. d'Immunologie.* 1960, Apr.–June, v. 24, No. 3, 388–99, 3 pls.

A very brief description is given of the apparatus and of the treatment and extraction of the mycobacteria from which the diffraction patterns were obtained; the strains used were H37Rv, BCG and unspecified saprophytes.

Examples of the patterns are shown but the patterns were not analysed because of their complexity and variability. So far, the study is recognized as being very incomplete, but the results form a base-line for future work; they show that the method is suitable for exploring the effects of drying, of different conditions of growth, of staining and of chemical extraction. However, although this method of examination yields information at the molecular level, and thus not obtainable by direct or electron microscopy, the information cannot be as precise as that obtained from crystalline, non-living structures. *S. R. M. Bushby*

TOGUNOVA, A. I., KARSANOVÁ, A. V. & STEPANCHENOK, G. I. **The Antigenic Properties of Suspensions of** *Mycobacterium tuberculosis* **exposed to Ultrasound.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 118–22, 1 fig. [Translated from Russian.]

Complement-fixation and agar-gel diffusion techniques were used in these antigenicity studies, and hyperimmune rabbit sera were used as the antibodies and phosphatide antigens, polysaccharide complexes and PPD as the standard antigens; the test antigens were from BCG and a variant, exposed to 800 and 1,200 kc/s for 2–4 hours.

The results showed that the treatment released specific soluble antigens which reacted with the serum to form precipitates, and that the precipitates in the diffusion plates coalesced with those formed from the known polysaccharide antigens of these test strains and from a virulent human strain. These soluble antigens also reacted with the complement-fixing antibodies.

S. R. M. Bushby

YAMAMURA, Y.; WALTER, A.; BLOCH, H. **Bacterial Populations in Experimental Murine Tuberculosis. I. Studies in Normal Mice** [YAMAMURA, WALTER & BLOCH]. *J. Infect. Dis.* 1960, Mar.–Apr., v. 106, No. 2, 211–22, 6 figs. [10 refs.] **II. Studies in Vaccinated Mice** [BLOCH, YAMAMURA & WALTER]. *Ibid.*, 223–9, 4 figs.

I. In the first of these papers the authors describe in detail their method of determining the total number of viable tubercle bacilli in mice infected with tubercle bacilli. The whole mouse is homogenized in a Waring blender and, after filtration through gauze, an aliquot of the filtrate is treated with caustic soda, to a final concentration of 1%, for 5 minutes. The viable count is then made by inoculating serial dilutions of the treated filtrate on to plates of Löwenstein-Jensen medium.

The method was shown to give reproducible results. After intravenous injection of H37Rv and the Ravenel strain, the number of viable bacilli dropped about 5-fold during the first week and then rose 100–1000-fold, depending on the size of the inoculum, the rise being higher with lower inocula; H37Ra differed in showing no increase. The number of bacilli recovered from mice that died from the infection was constant at about 10^8 bacilli, and in mice that survived, the number of bacilli remained constant at about 10^7 bacilli for several months.

Comparison of the distribution of the bacilli within the viscera showed that although at first the liver contained the highest number, later it was the lungs that contained the highest number; an initial increase also occurred in the number in the spleen and kidney.

II. In the second paper the results of 4 experiments are described. In the first, mice were vaccinated with 0·1 ml. of 1 in 10 dilution of a 14-day-old culture of BCG or 1 mgm. of phenol-killed BCG, and 28 days later they were challenged with the Ravenel strain. The numbers of viable bacilli recovered from the mice vaccinated with the killed bacilli were less than from unvaccinated mice, although they followed the same pattern; but in the mice given the living vaccine there was a more rapid initial fall with a slower recovery, although eventually, they were similar to those of the unvaccinated mice. Some of the vaccinated mice died relatively early, and as these animals contained as many bacilli as the unvaccinated mice, a possible heterogeneity of the challenge strain was suggested. This suggestion was apparently confirmed by the results of the second and third experiments for the bacilli recovered from a dead vaccinated mouse challenged with H37Rv were found to be more virulent than the stock cultures whereas those recovered from mice protected by the vaccine were less virulent. [It should be noted that the Ravenel strain was used for the challenge strain in the first experiment and H37Rv in the second one.] A fourth experiment showed that increase in the number of bacilli in vaccinated animals is proportional to the size of the challenge dose.

The authors conclude that vaccination increases the ability of mice to eliminate a certain proportion of the bacilli during the early phase of the infection, and that this proportion is determined by the nature and physiological state of the bacilli as well as the relative resistance of the host. *S. R. M. Bushby*

Stepanchenok, G. I., Togunova, A. I., Khatenever, M. L. & Kulikova, M. F. **The Influence of Ultrascund upon** *Mycobacterium tuberculosis.* *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 111–17, 5 figs. [Translated from Russian.]

According to the authors this study was aimed at solving problems connected with immunity; the ultrasonic apparatus used was the Soviet UL-1, which uses radiator disks of barium titanate piezoceramic producing intensities of 5 W/cm². at 400 and 2,400 kc/s and 10 W/cm². at 800 and 1,200 kc/s resonant frequencies. Suspensions of various strains of BCG and other attenuated strains of tubercule bacilli were exposed to the various frequencies for periods up to 4 hours and then examined by fuchsin stains and by electron microscopy.

Exposure to 400 kc/s for 30 minutes only divided the clumps into separate bacilli, but lengthening the time or increasing the frequency produced progressive disintegration of the bacilli, shown first by the appearance of acid-fast granules and non-acid-fast forms; eventually, with 1,200 kc/s, only a few acid-fast bacilli remained, the suspension then consisting mainly of amorphous material. The disintegration and the appearance of formed rounded bodies and structureless material were confirmed by electron microscopy. The viable counts made on the suspension showed that except for a rise after exposure to the low frequency, there was a fall in the number of viable units to 20–40% of the original number, but even after 6 hours' exposure, viable bacilli were still present. *S. R. M. Bushby*

Gray, D. F., Graham-Smith, Heather & Noble, J. L. **Variations in Natural Resistance to Tuberculosis.** *J. Hygiene.* 1960, June, v. 58, No. 2, 215–27, 2 figs. [22 refs.]

In the first of the experiments described in this paper, groups of 3 strains of mice, C57, HI and MUA, were infected intranasally with a small dose (150 viable units) of H37Rv. This dose was selected to avoid as far as possible pre-allergic deaths and yet cause extensive lung involvement [this *Bulletin,* 1959, v. 34, 163]. At weekly intervals the animals were tested for tuberculin hypersensitivity by injecting OT into the footpad, and the lungs of those dying were weighed. As 84% of the C57 mice were dead by the 37th day, whereas only 42% of the HI strain and 15% of the MUA had died, this strain would be regarded as highly susceptible, but judging from the increase in the weight of the lungs, the extent of the disease in all the dead mice, irrespective of the strain, was similar; none of the dead mice had developed hypersensitivity.

In the second experiment, groups of mice of the 3 strains were infected in a similar manner to those of the first experiment, and at approximately 3-day intervals a mouse of each strain was killed, its lungs weighed and a viable count made of the bacilli in the lungs. An examination of the lung weights showed that although there was a slightly greater initial rate of increase in those of the susceptible C57 strain, with a tendency for those of the resistant MUA strain to lag behind, the 3 groups were not separable at this stage. No dramatic change in the progress of the disease in the lungs occurred until the animals became tuberculin positive. Conversion occurred earliest in the MUA strain and latest in the C57 strain, and the lungs then became lighter and the number of viable bacilli, which had been increasing rapidly, showed a rapid decline.

Arguing from the results of these experiments and from those of other workers, the authors conclude that strains of mice do not vary in natural resistance to tuberculosis and that the observed differences are due to variations in the speed of onset of acquired immunity. They also point out that differences in apparent species susceptibility depend on the route of infection; when the intranasal route is used the mouse and rat are highly susceptible, whereas the guineapig is moderately and man highly resistant [*ibid,* 1956, v. 31, 143]. They suggest that species differences can be accounted for by observed phenomena, *e.g.* acquired immunity and hypersensitivity. *S. R. M. Bushby*

Mankiewicz, E. & Liivak, M. **Effect of** *Candida albicans* **on the Evolution of Experimental Tuberculosis.** [Correspondence.] *Nature.* 1960, July 16, v. 187, 250–51. [10 refs.]

The authors have previously shown that the presence of *Candida albicans* stimulates the growth of tubercle bacilli and that the enhancing factor is a polysaccharide [see this *Bulletin,* 1955, v. 30, 633; 1957, v. 32, 991; 1959, v. 34, 1170]. They now report that when 1 mgm. of the monilia or 50 mgm. [1 ml. of a 5% solution] of the polysaccharide was injected with H37Rv, into groups of 20 guineapigs, the tuberculous infection was more virulent, especially with the intact monilia. The increased virulence was shown by a higher mortality rate and an increased spread of the infection; the mortality after 6 weeks was 11 among those given the intact cells and 6 among those given the polysaccharide, whereas it was only 2 among those given the tubercle bacilli alone.

The polysaccharide resembles dextran, which is known to enhance the virulence of enterobacteria [*ibid,* 1954, v. 29, 851, *bis*], but as 1 mgm. of *C. albicans* contains only 0·1 mgm. of the polysaccharide, the amount of polysaccharide injected was exceedingly small unless the cells multiplied several times in the guineapigs before being destroyed by the animal. *S. R. M. Bushby*

Kölbel, H. Elektronenoptische Befunde zur Wirkung von Tween 80 auf die Zelle von *Mycobacterium avium.* [**Electron Microscopic Observations on the Action of Tween 80 on** *Myco. avium*] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 3, 371–82, 10 figs. [23 refs.]

Hedvall, E. **Atypical Acid-Fast Bacilli.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, Nos. 3/4, 248–60. [Numerous refs.]

This article consists mainly of a review of the literature concerning these organisms. The named species,

Mycobacterium fortuitum, Myco. balnei, Myco. ulcerans, Myco. glasgowi, Myco abscessus and *Myco. kansasi,* are dealt with in detail, and after brief references to the reports, starting with that of TIMPE and RUNYON [this *Bulletin,* 1955, v. 30, 170], to the so-called "atypical acid-fast bacilli", detailed descriptions are given of the characteristics by which Runyon classified these bacilli into the photochromogens, the scotochromogens, the non-photochromogens and the "rapid growers".

The author concludes by expressing some personal views. In his opinion a classification based on sensitivity to light is unsatisfactory, and the relationship between the presence of these bacilli and the lung changes which so closely resemble tuberculosis should be the subject of intensive research, not only by the bacteriologist but also by the lung specialist. Finally, the author summarizes what he considers to be the important criteria of diagnosing an infection by these bacilli:— the bacilli may be longer or shorter, and more pleomorphic than the tubercle bacillus; cultivation of acid-fast bacilli in sputum must always be attempted and the presence of drug resistance before treatment is highly suggestive of the strains; and the bacilli are usually strongly catalase-positive, neutral-red-negative, niacin-negative, and of low pathogenicity to animals.

S. R. M. Bushby

VIRTANEN, S. **A Study of Nitrate Reduction by Mycobacteria. The Use of the Nitrate Reduction Test in the Identification of Mycobacteria.** *Acta Tuberculosea Scandinavica.* 1960. Suppl. 48. 119 pp., 3 figs. [200 refs.]

This extensive study of nitrate reduction also includes a review of all the accepted tests used in the identification of mycobacteria. The actual experimental work was done on 791 strains of mycobacteria isolated from pathological specimens and on 52 various type-strains.

The reduction of nitrates was measured by incubating the organisms suspended in a strong M/45 phosphate buffer *p*H 7·0 + M/10 $NaNO_3$ for 2 hours. The presence of nitrate was estimated qualitatively or quantitatively by adding hydrochloric acid, sulphanilamide and N-(1-naphtyl)-ethylenediamine dihydrochloride. The bacilli were also submitted to extensive biochemical and virulence tests, the techniques of which are described in detail.

The author concludes that although all these strains of mycobacteria reduce nitrates, a quantitative estimation can be used for identifying the type. Human strains of tubercle bacilli, irrespective of virulence or sensitivity to isoniazid, are strong reducers, whereas bovine strains, including BCG, are weak reducers. The 43 strains of atypical acid-fast bacilli and the 12 strains of *Mycobacterium avium* gave variable results. The strains of *Myco. phlei, Myco. ranae,* and *Myco. smegmatis* were strong reactors, but those of *Myco. balnei, Myco. piscium* and *Myco. muris* were very weak reactors.

Between the *p*H range of 6 and 8, no significant variation in nitrate reduction was observed and the optimum temperature for reduction corresponded to that of optimum growth. Of the enzyme inhibitors examined, sodium azide gave some interesting results; this enzyme inhibits peroxidase and catalase and it markedly inhibited the nitrate reduction of H37Rv and, although more weakly, that of isoniazid-resistant, catalase-positive *Myco avium* and *Myco. phlei,* but it did not inhibit that of the isoniazid-resistant, catalase-negative human strains However, as it does not inhibit the reduction by the isoniazid-sensitive, catalase-positive H37Ra, catalase activity does not seem to be of decisive importance.

No reduction occurred with toluene-killed bacilli, which suggests either that mycobacteria do not possess independent nitrate-reductase or that the enzyme is not released from the cells by this treatment. Methods used for homogenizing sputum either markedly reduced or completely abolished the activity. Treatment of the bacilli with hydrogen peroxide abolished the activity of all the human strains, irrespective of catalase activity, but the effects on other myco-bacteria were variable; variation in oxygen tension had no effect on the reduction test but prolonged anaerobiasis abolished reduction activity. The presence of anti-tuberculous drugs or of substances that increase respiration, *e.g.* salicylic acid, also had no effect on the test. Growing the organisms in the presence of nitrate did not enhance the reduction activity, and apparently nitrate acts solely as an hydrogen-acceptor, for nitrates cannot be further reduced by mycobacteria; they are in fact toxic. No general correlation was found between ability to reduce tetrazolium or methylene blue and the ability to reduce nitrates.

The author concludes that the nitrate-reduction test, like the other biochemical tests used in the study of mycobacteria, is only complementary to the investigational procedures, but it is of particular value for differentiating human strains from bovine strains of tubercle bacilli.

S. R. M. Bushby

UYEDA, S. & NAKAMURA, K. Une mycobactérie chromogène constamment isolée du crachat d'une malade suspecte de tuberculose pulmonaire. [**A Chromogenic *Mycobacterium* repeatedly isolated from Sputum of a Patient suspected of Pulmonary Tuberculosis**] *Ann. Inst. Pasteur.* 1960, Aug., v. 99, No. 2, 319–21.

CIUCĂ, M., CALALB, G., SARAGEA, Alice, MAXIMESCO, Paula, STANICĂ, Ecaterina, IEREMIA, T., TUPA, Alexandra, MEITERT, Eugenia & STOIAN, Cecilia. Éco-systèmes "phage bactérie" et formes de "variation" de 565 souches de *Corynebacterium diphtheriae*—d'origine épidémique. Distribution des différents types. [**The Ecological System "Phage-Bacterium" and Forms of Variation among 565 Strains of *C. diphtheriae* from Epidemic Foci. Distribution of Types**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Mar., v. 19, No. 1, 59–68. [18 refs.]

An extensive investigation of all strains isolated in the course of 4 years in 11 different towns or districts is summarized in a table in which the data are given separately for different years.

Analysis of this table shows that in 4 of these areas here was a 90–100% incidence of *gravis* strains in certain years.

158 strains were isolated from patients or contacts in hese places and included 6 *mitis* and 1 *intermedius* train; 150 toxigenic and 131 lysogenic strains were found among these.

There were 7 areas in which no *gravis* strains were letected in a year. From these areas 163 strains (100 *nitis*) were isolated, and included 45 toxigenic and 11 ysogenic strains. More than half of these 163 strains were derived from carriers. The possible role of phage conversions in the changes of type observed in the different areas are discussed and had, it is suggested, an important role.

The most striking of all the observations recorded was n the foci T, A and H from which 66 strains 100% *gravis* were isolated from 5 patients and 61 contacts in 1958, whereas in 1959 a random sample of the population yielded 39 carriers of an unusual *mitis* strain. [The absence of any data with regard to the strains carried by non-contacts in 1958 makes conclusions about the possible or probable role of phage activities in such conversions very highly hypothetical.] *J. W. McLeod*

LAUTROP, H. **Laboratory Diagnosis of Whooping-Cough or *Bordetella* Infections.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 15–31. [Numerous refs.] [With an annex by B. W. LACEY on Cultural Diagnosis of Whooping Cough, 31–5.]

This is a clear and comprehensive description of the methods employed in the laboratory diagnosis of *Bordetella* [*Haemophilus*] infections. Three closely related organisms may be involved in whooping-cough infections viz:—*Bordetella pertussis* (formerly *Haemophilus pertussis*) responsible for 95% of cases, *Bordetella parapertusis* responsible for 5% of cases, and *Bordetella bronchiseptica* (*Brucella bronchiseptica*), responsible for 0·1% of cases.

Very often isolation and identification of *Bordetella* organisms depends upon the experience of the investigator. Two methods are described in this paper. The first, the conventional one, involves the use of Bordet-Gengou medium and requires considerable experience on the part of the investigator. The second employs a strongly selective medium described by B. W. LACEY in the appendix to this paper. Lacey's diamidine—penicillin—fluoride medium [this *Bulletin,* 1955, v. 30, 2] keeps longer than Bordet-Gengou (B-G) medium and will give successful results when the investigator is not particularly experienced. It is suggested that this procedure will be advantageous in laboratories which receive only a small number of specimens for investigation. Specimens may be collected by peroral or pernasal swabs. Unless a carrier medium is available, the swabs should be plated immediately because the survival time of *Bordetella* organisms is short. The cough plate method is not so effective as the swab method, but has the advantage that the plate acts as a carrier medium and the organisms will survive. This allows specimens to be taken at home. Specimens are incubated at 35°C. in a humid atmosphere. The B-G medium should contain 50% blood and penicillin in a final concentration of 0·5 unit. Human, rabbit, sheep, or horse blood may be used—all have similar growth-promoting capacity. Primary examination of plates involves searching for typical *Bordetella* colonies and the microscopic examination of Gram-stained films. There is a detailed description of the colonial and morphological appearances of the 3 species of *Bordetella* and of the biochemical tests which will differentiate between them. Final identification is by serological tests. All *Bordetella* species have the same O antigen but have different K antigens. Strains within a species have a major K antigen which is identical in all strains of the species, and also several minor K antigens which may be shared by other strains. Tube agglutination is preferred to slide agglutination and is best carried out at room temperature on a shaking machine and read after 1 hour. *May F. McCallum*

PICKETT, M. J. & LAUGHNER, S. M. **Screening for *Salmonella* with Bacteriophage.** *Amer. J. Clin. Path.* 1960, Apr., v. 33, No. 4, 298–302. [10 refs.]

Although comparatively little has been published about the use of FELIX and CALLOW's salmonella phage "O-1" [this *Bulletin,* 1943, v. 18, 865] for the routine generic identification of members of the group, the possibilities of exploiting the method have been considered by a number of workers in this field. Most experienced workers in intestinal bacteriology, however, employ serological screening methods for salmonella-group identification that are simple, reliable and extremely rapid, and it is generally not felt that phage-screening offers any great advantage for the preliminary study of salmonella-like colonies.

The present paper describes a rapid method for phage-screening salmonellae which employs a pool of this "O-1" salmonella phage and an adapted "Group D" phage of WASSERMANN and SAPHRA [this *Bulletin,* 1955, v. 30, 630]. In place of the usual broth culture for the preparation of the bacterial lawn for the phage tests the authors transfer the suspected colony directly to the test medium with a small loop by which means it is spread as a small lawn 5 × 20 mm. A number of lawns representing different colonies can thus be accommodated on a plate and each lawn is then spotted with the divalent phage preparation. The result can usually be read after 4 hours' incubation. The authors speak well of the sensitivity and specificity of the test [but it seems doubtful if their claim for it as a labour-saving device can be justified]. *H. J. Bensted*

SCHOLTENS, R. T. De faagtypering van *Salmonella paratyphi B* in Nederland. [**Phage Typing of *Salmonella paratyphi B* in the Netherlands**] *Nederl. Tijdschr. v. Geneesk.* 1960, May 21, v. 104, No. 21, 1029–38, 6 figs. [16 refs.] English summary (6 lines).

The author has previously [this *Bulletin,* 1951, v. 26, 177] developed a natural method of phage typing which

is based on the additional feature of the isolation and identification of the lysogenic phage contained in the organism, and in the present work this method is compared with the standard method of FELIX and CALLOW [this *Bulletin*, 1943, v. 18, 865; 1951, v. 26, 1116] in the examination of strains of *Salmonella paratyphi B*. The natural system is first set forth in a table; the author then points out that phages considered by Felix and Callow to be unstable are not included in the natural system, and Salm. Java also cannot be typed by it. However, the natural system can accommodate types which cannot be distinguished by the standard method, and this can be of epidemiological value. The type Sittard in particular, which causes epidemics in Holland, can be identified by the natural system, whereas by the standard method it may be identified as 3aI or Beccles. Other examples of incorrect identification are given in a table. The practical applications of the natural method are described; 444, 434, 263 and 379 strains of *Salm. paratyphi B* were isolated in Holland in the years 1954–57 respectively, and of these the type Taunton-Kampen constituted 29%, type 1 13%, Jersey 10%, 3aI-Leeuwerden 9%, BAOR 7%, 3a 6%, Dundee 6%. Beccles-Meppel 5%, 3aI-Schiedam 3%, Midwoud 2%, Sittard 1%, 3b 1% and types 22 and 3al var. 1–2 1%. *Anne Tothill*

MIYAKE, T. & DEMEREC, M. **Proline Mutants of *Salmonella typhimurium*.** *Genetics.* 1960, June, v. 45, No. 6, 755–62, 1 fig. [13 refs.]

WESTPHAL, O., KAUFFMANN, F., LÜDERITZ, O. & STIERLIN, H. Zur Immunchemie der O-Antigene von Enterobacteriaceae. III. Analyse der Zuckerbausteine kreuzreagierender *Salmonella-*, *Arizona-* und *Escherichia*-O-Antigene. [**Immunochemistry of the O-Antigens of Enterobacteriaceae. III. Analysis of the Sugar Components of Cross-reacting O-Antigens of *Salmonella, Arizona* and *Escherichia*]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 3, 336–42. [12 refs.]

The English summary appended to the paper is as follows:—

"The sugar constituents of 29 *Salmonella, Arizona,* and *Escherichia* O antigens out of 11 cross-reacting groups were qualitatively analyzed. Serologically identical or closely related O antigens were found to be mostly built up of the same sugar constituents, thus belonging to the same chemotype.

"Two pairs of cross-reacting *Salmonella/Pseudotuberculosis* O antigens were also analyzed.

"With the production of the antigenic factor 48 in *Salmonella* group Y the occurrence of colominic acid (poly-neuraminic acid) was found to be tightly linked. This is also true for a colominic acid-producing *Citrobacter* strain, the polysaccharide of which is cross-reacting with the *Salmonella* O 48 antigen.

"The significance of such analyses for sero-diagnostic, classifying, biochemical, as well as genetic aspects is pointed out."

LINTON, K. B. **The Colicine Typing of Coliform Bacilli in the Study of Cross-Infection in Urology.** *J. Clin. Path.* 1960, Mar., v. 13, No. 2, 168–72, 3 figs. [11 refs.]

The author examined 314 strains of coliform bacilli (79 *Klebsiella* and 235 *Escherichia coli*), most of which had been isolated from urines, for evidence colicine activity—colicine production or colicine sensitivity. The methods employed were modifications of the basic techniques described by FREDERICQ, *et al.* [this *Bulletin*, 1947, v. 22, 533]. Standard sensitive strains of *E. coli* were used for the detection of colicine production by the strains under test, first by screening and finally by typing in accordance with the activity pattern obtained with the 10 standard sensitive strains. The sensitivity tests were similarly carried out with 10 standard producer strains.

Only one of the 79 *Klebsiella* strains showed any colicine activity, being colicine sensitive. Of the 235 strains of *E. coli* examined 97 were found to be colicine producers and 172 were colicine sensitive (65 were both producers of and sensitive to, colicines; 31 were neither).

The value of colicine typing, at least by the methods employed by the author, appears to be limited in epidemiological studies owing to the fact that they cannot be applied to the *Klebsiella* group of organisms which is so frequently responsible for hospital cross-infections. The method has, however, proved to be useful in investigating some of the *E. coli* infections. *H. J. Bensted*

COX, R. A. & LITTAUER, U. Z. **Properties of Low Molecular Weight RNA from *E. coli*.** [Correspondence.] *J. Molecular Biol.* London. 1960, Aug., v. 2, No. 3, 166–8, 2 figs. [12 refs.]

ROGERS, D. & REITHEL, F. J. **Acid Phosphatases of *Escherichia coli*.** *Arch. Biochemistry.* 1960, July, v. 89, No. 1, 97–104, 4 figs. & 1 diagram. [14 refs.]

ELBERG, S. S., MASCARENHAS, Patricia & FONG, J. **Response of Peritoneal Exudate Cells to *Brucella melitensis*. Influence of Nature of Inflammatory Irritant.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 295–7.

"A comparison has been made of the effect of several irritants on response of mononuclear cells from rabbit's inflamed peritoneum. Animals injected intraperitoneally with mineral oil or a suspension of killed *B. melitensis* stimulated accumulation of peritoneal monocytes whose behaviour was identical towards living *B. melitensis, i.e.* brucellae were cytolytic for normal rabbit monocytes but not for immune rabbit monocytes. Dextran and casein stimulated exudation of relatively insusceptible monocytes. Glycogen induced exudation of a relatively fragile monocyte, the susceptibility of which to Brucella parasitization was increased by the *immune state* of host animal."

Aronson, M. & Bichowsky-Slomnicki, L. **Temperature and pH-Dependent Changes of Electrophoretic Mobility of** *Pasteurella pestis*. *J. Bacteriology*. 1960, May, v. 79, No. 5, 734–40, 3 figs. [14 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 1166.]

Kaufman, L. & Weaver, R. H. **Use of Neutral Red Fluorescence for the Identification of Colonies of Clostridia.** *J. Bacteriology*. 1960, Feb., v. 79, No. 2, 292–4.

The authors, by using Difco liver veal agar with 0·004% of neutral red incorporated and making a sandwich plate with the inoculated layer of medium between two uninoculated layers, find that after incubation in an atmosphere of hydrogen all clostridia growing show zones of golden yellow fluorescence within 24 hours in ultra-violet light and within 48 hours in daylight.

This effect was obtained also with two non-sporing anaerobes but not with anaerobic cocci. It was not obtained with any aerobic or facultatively aerobic micro-organism.

The relationship of this phenomenon to the reducing potential developed by bacteria is discussed.

J. W. McLeod

Takagi, A., Kawata, T. & Yamamoto, S. **Electron Microscope Studies on Ultrathin Sections of Spores of the** *Clostridium* **Group, with special reference to the Sporulation and Germination Process.** *J. Bacteriology*. 1960, July, v. 80, No. 1, 37–46, 20 figs. [16 refs.]

Fulthorpe, A. J. & Thomson, R. O. **Antigenic Efficiency of Tetanus Toxoids modified by Excess Formalin or by Heat and Phenol.** *Immunology*. Oxford. 1960, Apr., v. 3, No. 2, 126–34, 1 fig. [11 refs.]

Treatment of tetanus toxoid with excess formalin or with heat in the presence of 0·5% phenol reduces its antitoxin-combining power [this *Bulletin*, 1959, v. 34, 580]. This can be demonstrated by the total combining power tests in mice and also by the haemagglutination inhibition test, but the customary flocculation test to indicate the potency of toxoid preparations in terms of antitoxin-combining power gives results which greatly underestimate this reduced power. The quantity of formalin required to convert toxin to toxoid varies according to the preparation. High purity toxoid is more susceptible to formalin denaturation than cruder preparations; toxins from which amino-acids and other dialysable formalin-fixing compounds, present in the nutrient culture media, have been removed require very small amounts of formalin for conversion to toxoid. But purity of a toxoid in terms of Lf/mgm. protein N is not necessarily an indication of antigenicity: indeed tetanus toxoids of widely different purity as expressed as Lf/mgm. protein N may be equally potent in terms of antigenicity.

Heating tetanus toxoid at 50°C. in the presence of 0·5% phenol for varying periods causes progressive loss of antitoxin-combining power. As long as the heating is not prolonged there is, however, a significant increase in antigenicity but prolonged heating results in a decreased response. It is suggested that the short period heating destroys the heat labile non-specific fraction which may lead to an improvement in the quality of the preparation.

H. J. Bensted

Wright, G. G., Duff, J. T., Fiock, Mary A., Devlin, H. B. & Soderstrom, R. L. **Studies on Immunity to Toxins of** *Clostridium botulinum*. **V. Detoxification of Purified Type A and Type B Toxins, and the Antigenicity of Univalent and Bivalent Aluminum Phosphate Adsorbed Toxoids.** *J. Immunology*. 1960, Apr., v. 84, No. 4, 384–9, 1 fig. [17 refs.]

Alcohol precipitated fractions obtained by the method of Duff, *et al.* [this *Bulletin*, 1957, v. 32, 1109] were used and contained 200 × 10^6 LD50/mgm. N in case of toxin A and rather more in case of toxin B.

The authors studied the rates of formaldehyde detoxification for both toxins, using 0·6% at *p*H 5·5 and 35°C. 16 days were required for A toxin and 20 for B toxin. The rate of detoxification, at first very rapid, was much slowed down in the second week and this was more so if tests were made on guineapigs instead of mice.

These observations led the authors to speculate on the possibility of the existence of two varieties of toxin, although post mortem evidence indicated botulism as the cause of death also in the animals succumbing to partially inactivated toxin.

Aluminium-adsorbed toxoid was prepared by a modification of Holt's methods and mice immunized with such products were challenged with "acid-precipitated whole culture toxin".

The number of LD50 doses of toxin resisted increased from the third to the fifth week after immunization, but more so with B toxin.

There was also a marked advance in resistance with increased dose of toxoid, *i.e.* the number of doses resisted was increased 100–200-fold as the immunizing dose was raised from 0·03 Lf to 3 Lf. Titrations of units of antitoxin in the sera of animals, rabbits immunized with bivalent (A and B) aluminium-phosphate-precipitated toxoids showed titres of 0·4 to 2·7 units of antitoxin/ml. of serum after 50 days. These toxoid preparations were relatively stable for 3 years at 4°C.

J. W. McLeod

Broom, J. C. & Coghlan, Joyce D., with the assistance of E. Kmety. *Leptospira bratislava* **isolated from a Hedgehog in Scotland.** *Lancet*. 1960, June 18, 1326–7. [13 refs.]

The first isolation of *Leptospira bratislava* in Britain is reported. the source was the kidney of a hedgehog

caught near Edinburgh. No agglutinins against *L. bratislava* could be detected in this hedgehog's serum; and the authors made similar observations in a recent survey of wild rodents [this *Bulletin*, 1959, v. 34, 222]. The serum did, however, agglutinate 6 out of 7 serotypes with which it was tested: *L. sejroe* and *L. bataviae* at a titre of 1:100; and *L. icterohaemorrhagiae, L. pomona, L. grippotyphosa,* and *L. ballum* at 1:30; while *L. canicola* did not agglutinate. These findings re-emphasize the fallibility of leptospiral surveys based on serological tests alone.

The first strains of leptospires isolated from hedgehogs by KMETY in Slovakia in 1953 (PLESKO *et al.*, *Československ. Epidemiol., Mikrobiol., Immunobiol.*, Prague, 1960, v. 9, 12) were found to belong to a new serotype, related to the australis A group, which Kmety named *L. bratislava*. Leptospires isolated later from hedgehogs in the U.S.S.R. and Poland, which were named *L. erinacei europaei*, proved to be identical with *L. bratislava*. Kmety found that 14 of 17 hedgehog strains in Slovakia were *L. bratislava* and that 35% of hedgehog sera obtained in his survey agglutinated this serotype with titres of 1:100 to 1:50,000. *L. bratislava* has been isolated only twice from sources other than hedgehogs: once from a bank vole (*Clethrionomys glareolus*), and once from the blood of a patient [clinical details are not stated].

L. bratislava now joins *L. icterohæmorrhagiae, L. canicola, L. ballum,* and strains related to *L. saxkoebing* and *L. sejroe,* as representatives of the genus *Leptospira* known to be indigenous in Britain.

L. H. Turner

BACTERIOPHAGES

HATANO, M., NAKAMURA, K. & KUROKAWA, M. **Isolation of a New Temperate Phage causing the Lysogenic Conversion in** *Corynebacterium diphtheriae*. *Japanese J. Microbiol.* 1959, July, v. 3, No. 3, 301–11, 5 figs. [19 refs.]

21 phage strains were isolated from 55 strains of toxigenic *Corynebacterium diphtheriae,* types *gravis, intermedius* and *mitis*. The phage strains fell into 2 groups. One was almost identical with phage β [GROMAN and EATON, this *Bulletin*, 1956, v. 31, 743] while the other, designated κ, though sharing many properties with β, differed in host range. β and κ phages had similar rates of adsorption and latent periods; their UV inactivation curves were similar but β phages were slightly more resistant to temperatures of 56°–60°C. than κ; cross-neutralization tests revealed no serological differences. Both kinds were temperate phages, causing their host to become toxigenic by lysogenic conversion. Each type produced plaques on an indicator strain lysogenic with the other type.

Of epidemiological interest, there seemed to be an association between the phage type and the area from which the bacterial strain carrying it was originally isolated, although strains were isolated at different times.

Janice Taverne

ARBER, W. **Polylysogeny for Bacteriophage Lambda.** *Virology*. New York. 1960, May, v. 11, No. 1, 250–72. [28 refs.]

Escherichia coli K 12 cells can be made doubly lysogenic with different λ mutants by several techniques. These have been investigated, together with the stability of the prophages in the doubly lysogenic strains, their situation on the bacterial chromosome and the properties of the phages released by induction.

Most subclones from cells surviving simultaneous infection with 2 λ strains of different host range were lysogenic for both strains. When one lysogenic strain was superinfected with the other phage, doubly lysogenic strains were obtained only rarely, but more often if the superinfecting phage was irradiated with UV light before adsorption. Upon induction, doubly lysogenic cells liberated phage of both kinds, the proportions varying with the strains, as well as recombinants. Phenotypic mixing was also observed in the lysates.

The location of the prophages on the bacterial chromosome was determined by bacterial recombination experiments and by transduction with phage P1. Both prophages were found to be attached in the characteristic λ region, close to the *gal* markers, and they could not be separated.

Janice Taverne

ARBER, W. **Transduction of Chromosomal Genes and Episomes in** *Escherichia coli*. *Virology*. New York. 1960, May, v. 11, No. 1, 273–88, 2 figs. [22 refs.]

Phage P1 grown in *Escherichia coli* K 12 cells having certain nutritional requirements transduced the gene regions controlling these requirements to recipient cells at frequencies of about 1 in 10^4 to 10^5 phage particles. UV irradiation of P1 before transduction increased the frequency of stable transduction. P1 grown in cells lysogenic for λ phage transduced the prophage to non-lysogenic cells, and P1 grown in F^+ or HFr strains transduced the fertility factor F to F^- cells at similar rates. The transfer of λ prophage to sensitive cells led to "transfer induction" followed by phage multiplication and release of new λ particles, except rarely, when stable integration led to the establishment of lysogeny. The transfer of F converted the recipient cell into F^+. The rate of transfer of these *episomes* [inherited factors which may be connected to the chromosome or exist separately in an autonomous state (JACOB and WOLLMAN, *C. R. Acad. Sci.*, 1958, v. 247, 154)] was not increased by UV irradiation. Irradiation reduced the survival of the

episomes exponentially; λ prophage was lost at the same rate as free phage and F showed comparable UV sensitivity. *Janice Taverne*

HERSHEY, A. D. & BURGI, Elizabeth. **Molecular Homogeneity of the Deoxyribonucleic Acid of Phage T2.** *J. Molecular Biol.* London. 1960, Aug., v. 2, No. 3, 143–52, 9 figs.

BEUMER, J. & DIRKX, J. Isolement de substances réceptrices des bactériophages chez les *Shigellae.* [**Isolation from Shigellae of Receptor Substances for Bacteriophages**] *Ann. Inst. Pasteur.* 1960, June, v. 98, No. 6, 910–14. [16 refs.]

The English summary appended to the paper is as follows:—

"Receptor substances for the phages of the lysogenic strain B. Lisbonne were prepared from *Shigellae* strains. Extraction in the cold with 5 p. 100 trichloracetic acid was found convenient for isolating the receptors from the S strains. Those from the R strains could be extracted by treating the bacteria suspended in water with an equal volume of 90 p. 100 phenol at 68°C. The receptor substances contain sugars and fatty acids and might be lipo-polysaccharids. Purification and chemical analysis of these receptors are in progress."

PIETRZYKOWSKA, I. **Induction of the Lysogenic Phase by RNase.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 6, 223–6, 2 figs.

A lysogenic strain of *Bacillus megaterium* (strain W899) was incubated with RNase, the cells were washed, and free phage was titrated at intervals. While the optical density of the culture remained constant, the amount of free phage increased. Although the latent period was about twice as long as that which followed UV induction, the curves showing phage synthesis were similar. In control cultures incubated without RNase free phage also increased, spontaneously, but was accompanied by an increase in optical density.

Janice Taverne

BARRICELLI, N. A.; DOERMANN, A. H. **An Analytical Approach to the Problems of Phage Recombination and Reproduction. I. Multiplicity Reactivation and the Nature of Radiation Damages** [BARRICELLI]. *Virology.* New York. 1960, May, v. 11, No. 1, 99–135, 6 figs. [29 refs.] **II. High Negative Interference** [BARRICELLI & DOERMANN]. *Ibid.*, 136–55, 2 figs. [11 refs.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

SYKES, J. A. & MOORE, E. B. **A Simple Tissue Culture Chamber.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 2, 288–97, 7 figs. [15 refs.]

A simple heat-sterilizable tissue culture chamber is described which enables cells to be examined satisfactorily under high magnification with either a conventional or phase contrast microscope. The apparatus is described in detail. It has advantages since it is easy to make and assemble, is heat-sterilizable and should be easy to use. *A. J. Beale*

BUCCA, M. A., CASEY, Helen L. & WINN, J. F. **Method of Concentration of Viral Diagnostic Reagents using Hydrophilic Agents.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 247–50. [14 refs.]

WOOLRIDGE, R. L., JACKSON, Elizabeth B. & GRAYSTON, J. T. **Serological Relationship of Trachoma, Psittacosis and Lymphogranuloma Venereum Viruses.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 298–301. [15 refs.]

"Sera from patients with trachoma, psittacosis and lymphogranuloma venereum were tested in the complement fixation test with both 'purified' elementary body antigens and boiled phenolized group antigens made with each of the 3 viruses. Group antigen prepared with trachoma virus reacted similarly to group antigens made with psittacosis and lymphogranuloma venereum viruses. The trachoma elementary body antigen reacted only with sera from trachoma patients. Psittacosis and lymphogranuloma venereum elementary body antigens failed to react with trachoma serum but did react about equally with sera from both psittacosis and lymphogranuloma venereum patients. It is concluded that trachoma virus contains the group antigen of the P-LV group and in addition a specific antigen which permits its serologic differentiation from the agents of psittacosis and lymphogranuloma venereum."

DOUGHERTY, R. M., MCCLOSKEY, R. V. & STEWART, R. B. **Analysis of the Single Dilution Method of Titration of Psittacosis Virus.** *J. Bacteriology.* 1960, June, v. 79, No. 6, 899–903, 3 figs.

It is shown in this paper that the susceptibility of embryonated hen's eggs for psittacosis virus varies significantly with eggs obtained from different flocks or from the same flock at different times. The authors point

out that psittacosis virus titrations depending alone on survival time are only comparable, therefore, if done at the same time with eggs from the same source.

S. P. Bedson

POLLARD, M., STARR, T. J., TANAMI, Y. & MOORE, R. W. **Propagation of Trachoma Virus in Cultures of Human Tissues.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 223–5, 2 figs. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 1218.]

JOKLIK, W. W., ABEL, Pamela & HOLMES, I. H. **Reactivation of Poxviruses by a Non-Genetic Mechanism.** [Correspondence.] *Nature.* 1960, June 18, v. 186, 992–3, 1 fig.

Inactivation of pox viruses by heat cannot result from destruction of DNA since mixed infection with heated and unheated virus of different strains gives rise to progeny of both strains, and sometimes to recombinants (JOKLIK *et al., Virology,* 1960, v. 11, 168). To prove that heat injures only the protein and that this is restored by the reactivating virus, cells of the chick chorioallantoic membrane were doubly infected with a heat-inactivated strain and a strain whose DNA had been specifically destroyed. A rabbit pox mutant, RP*u,* which produces white pocks, was heated and mixed with the wild type, RP*u*$^+$, producing haemorrhagic, ulcerated pocks, which had been inactivated with different doses of nitrogen mustard, di(2 chloroethyl)methylamine. This compound combines with the DNA of phage without affecting the protein coat [LOVELESS and STOCK, this *Bulletin,* 1960, v. 35, 400]. The infectivity of RP*u*$^+$ was destroyed by nitrogen mustard by a one-hit process, as was its ability to reactivate heated virus, but the latter was more resistant. Analysis of the progeny showed that some RP*u*$^+$ particles whose DNA had been destroyed, judged by the absence of red, ulcerated pocks, were still able to reactivate heated RP*u* particles. Thus the reactivating virus must replace some non-genetic material which has been destroyed by heat.

Janice Taverne

WHEELER, C. E. & CANBY, C. M. **Relationship of Temperature to Inapparent Infection of HeLa Cells with Herpes Simplex Virus.** *J. Bacteriology.* 1960, May, v. 79, No. 5, 657–60, 9 figs. [10 refs.]

" Herpes simplex virus production either did not occur or took place very slowly in HeLa cultures nourished with a maintenance medium and incubated at 25°C. for 9 days.

" Elevation of the temperature of incubation to 35°C. resulted in prompt production of herpes virus in herpes-infected HeLa cultures which had been incubated at 25°C. for as long as 6 days."

HORNE, R. W., WATERSON, A. P., WILDY, P. & FARNHAM, A. E. **The Structure and Composition of the Myxoviruses. I. Electron Microscope Studies of the Structure of Myxovirus Particles by Negative Staining Techniques.** *Virology.* New York. 1960, May, v. 11, No. 1, 79–98. 9 figs. [31 refs.]

Influenza virus (egg-adapted WSE variant of the A strain, PR8 and A/Persian Gulf/2/52 strains), Sendai virus, NDV, fowl plague virus (Rostock strain) and mumps virus (Enders strain) were prepared in the allantoic sac of embryonated eggs. These viruses were concentrated and purified either by differential centrifugation or by adsorption to and elution from red cells. Equal volumes of virus suspensions and 2% phosphotungstic acid (*p*H adjusted to 7·0) were sprayed directly onto carbon-coated supporting grids and examined in the Siemens Elmiskop electron microscope at instrumental magnifications of 8,000 and 40,000. Constant features of these preparations were an outer membrane approximately 100–150 Å thick, covered by a series of projections (80–100 Å long and a centre-to-centre distance of 70–80 Å), which enclosed a structure of mottled or whorled appearance.

Particles of mumps virus, some more than 5,000 Å wide, disrupted spontaneously to reveal a coiled hollow tube. The mean diameter of this tube was 170 Å and that of its hole 40–50 Å and there was a regular periodicity of 50 Å along the axis. Particles of NDV had diameters approaching 1,500 Å with intact virus and about 2,000 Å with disrupted or collapsed virus; although smaller than mumps virus they had an internal helical structure of the same type and diameter. Sendai virus particles were of similar diameter to those of mumps but the inner component was of even greater interest since it suggested the existence of a double helix. The three viruses mentioned fell into one group since they disrupted easily, were larger than the viruses of fowl plague and influenza and less pleomorphic. Fowl plague virus and classic influenza virus, which were not morphologically different, had diameters between 800 and 1,800 Å. Despite this pleomorphism few disrupted particles were seen so that the size and arrangement of a tightly packed inner structure of round spiral appearance could not be determined. However, ether-treated preparations of these viruses have revealed a helical inner component, possibly double stranded. Preparations of incomplete influenza virus (WSE) varied in shape from elongated to spherical forms and in size (up to 5,000 Å), but the characteristic outer membrane was retained. No internal structure was noted in the filamentous Persian Gulf strain of influenza virus. Finally, threads about 3,000 Å long consisting of a series of spherical bodies (50–60 Å diameter; mean separation distance of 80 Å), seen in many preparations, were believed to be molecules of mucoprotein inhibitor.

[The electron micrographs presented in this paper are very fine indeed. The authors write from Cambridge, England.] *D. Taylor-Robinson*

HANIG, M. & STEIM, J. M. **Physical Incompleteness of Influenza Virus propagated in De-Embryonated Eggs.** *Nature.* 1960, July 2, v. 187, 40–42, 1 fig. [17 refs.]

PR8 virus was grown in de-embryonated eggs and the resultant virus was purified by ultracentrifugation or by adsorption and elution on red cells. The purified material was examined in the analytical ultracentrifuge, the sedimentation constant was estimated at various concentrations and extrapolated to zero concentration. Where the eggs were inoculated with virus seed diluted 10^{-5}, the virus produced was "complete" with over 10^6 EID50 per haemagglutinin (HA) unit and this virus sedimented fast, $S\ w/20\,\infty = 697 \pm 4{\cdot}3$. When the inoculum was diluted 10^{-1} the virus produced was incomplete with about 10^3 EID50 per HA unit—and this virus sedimented slowly, $S\ w/20\,\infty = 541 \pm 4{\cdot}1$. The authors emphasize that there was no overlap between the values obtained with "complete" and "incomplete" preparations, and state that when embryonated eggs were inoculated with virus diluted 10^{-3} the virus produced sedimented as two distinct components corresponding to the "fast" and "slow" components described above.

D. A. J. Tyrrell

SPENCE, L. **Kaolin Treatment of Sera for Removal of Nonspecific Inhibitors to Asian Strains of Influenza Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 425–7.

It is regretted that the author's summary was incorrectly reproduced in this *Bulletin*, 1960, v. 35, 709. The correct version is as follows:—

"The use of kaolin for treatment of sera in diagnosis of Asian influenza cases by haemagglutination-inhibition test is reported. Comparison of kaolin treatment with other methods in common use is made. The advantages of kaolin treatment over other technics warrant further trial of the method."

LANGE, F. C. Über die toxische und antigene Wirksamkeit von Viren. III. Mitteilung: Quantitative Untersuchungen über die Bildung hämagglutinationshemmender Antikörper. [**The Toxic and Antigenic Activity of Viruses. 3rd Communication: Quantitative Studies on the Production of Haemagglutination Inhibiting Antibodies**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 2–16, 4 figs. [17 refs.]

The author has investigated the relationship between the production of inhibiting antibody and the dose of virus in guineapigs immunized with influenza virus adsorbed on gamma-aluminium oxide. 3 groups of 5–10 animals were given a strain of type A2 virus by daily intraperitoneal injection in 3 dose levels covering over a 400-fold range and investigated over a period of 22 days. A somewhat more rapid appearance of antibody was noted with the highest dose, which caused the death of most of the animals from toxicity. Similar results were obtained with the PR8 strain. The antibody response to a second infection with virus was also studied [for part II, see this *Bulletin*, 1960, v. 35, 709]. *D. J. Bauer*

DRESCHER, J. Über Adsorptionsvorgänge bei Virusarten. V. Mitteilung: Untersuchungen über die Adsorption von A/2/Sing/1/57-Influenzavirus an γ-Aluminiumoxyd. [**Adsorption Phenomena in Viruses. Fifth Communication: Investigations of the Adsorption of A/2/Sing/1/57-Influenza Virus Strain on γ-Aluminium Oxide**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 17–28, 1 fig. [13 refs.]

An investigation has been made of the rate of adsorption of the A2/Sing/1/57 strain of influenza virus on gamma-aluminium oxide at 4°C.; the process was found to obey the Freundlich adsorption isotherm, and the constants of the adsorption equation were determined with different amounts of adsorbent and at different *p*H values. Virus was adsorbed up to 24 hours after adding the aluminium oxide; an equilibrium was then attained, and no further adsorption took place over a period of 10 days. Adsorption was independent of *p*H over the range 6·3–7·8. *D. J. Bauer*

TAKÁTSY, G. & BARB, Katalin. **Studies on the Variation in the Antigenic Structure of Influenza A-2 Virus.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 2, 131–5, 2 figs.

CRAIGHEAD, J. E., COOK, M. Katherine & CHANOCK, R. M. **Infection of Hamsters with Para Influenza 3 Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 301–4.

"Hamsters were infected by the intranasal route with para influenza 3 virus. One tissue culture infectious dose was sufficient to infect hamsters. Quantity of virus produced in the lung was the same, $10^{5.9}$ to $10^{6.9}$, during infection with virus grown only in tissue culture or virus passaged in hamsters. Infected hamsters developed high levels of CF antibody specific for para influenza 3 virus."

VAN DER VEEN, J. & PRINS, A. **Studies of the Significance of the Recall Phenomenon in the Antibody Response to Adenovirus Vaccine and Infection.** *J. Immunology.* 1960, June, v. 84, No. 6, 562–8, 2 figs. [25 refs.]

This investigation was carried out on 3 groups of recruits who entered a military camp in the Netherlands in April 1955 and February and December 1958. In the December intake, 73 randomly selected recruits were each given 1 ml. of monovalent type 4 or 7 vaccine (Lederle) intramuscularly. Sera collected just before and 10 days after vaccination were titrated in neutralization tests against adenovirus types 3, 4, 7 and 14.

A homotypic antibody response occurred in approximately 80% of 37 men who were given type 4 vaccine, the geometric mean titre increasing 25-fold; there was

no antibody rise against adenovirus type 7 and a slight increase against types 3 and 14. The mean antibody titre against type 7 adenovirus increased 100-fold in 36 recruits who received type 7 vaccine and there was also a significant increase in titre against heterologous types 3 and 14 in 83% and 61% of recruits respectively. In contrast, complement-fixing antibody increased only 4-fold in response to types 4 and 7 vaccine; there was no significant increase of antibody in 104 recruits, selected at random, who did not receive vaccine. Type-specific neutralization tests on sera from the 3 groups of recruits showed that antibody to types 3, 7 and 14 was common before or at the time of vaccination whereas type 4 antibody was less prevalent. A heterotypic antibody rise occurred more frequently when the initial serum contained heterotypic neutralizing antibody than when it did not.

The authors consider that these facts support the concept of a recall phenomenon. *D. Taylor-Robinson*

HARTLEY, J. W. & ROWE, W. P. **A New Mouse Virus apparently related to the Adenovirus Group.** *Virology*. New York. 1960, July, v. 11, No. 3, 645–7.

ZWARTOUW, H. T., TAYLOR-ROBINSON, D. & WESTWOOD, J. C. N. **Growth of High-Titer Poliovirus in Nutrient-Free Saline Suspensions of ERK Cells.** *Virology*. New York. 1960, Apr., v. 10, No. 4, 393–405, 2 figs. [15 refs.]

The authors investigated the conditions required for the growth of high-titre poliovirus in cell suspensions using the Brunhilde strain of type 1 poliovirus at a multiplicity of 2 and ERK cells at a concentration of 10^7 per ml. Under these conditions the yield was as high when Earle's saline without glucose was used, adjusted to a *p*H 6·8–7·7 with sodium bicarbonate in the range 0·07–0·22%. Higher levels of bicarbonate caused lower poliovirus yields but this could be reversed by the addition of glucose. Tris (tris(hydroxymethyl)aminomethane) buffer was toxic at 0·05 M: at 0·025 M yield was depressed but restored by the addition of 0·013 M $NaHCO_3$.

Intracellular virus reached a peak at 12 hours and extracellular virus at 24 hours when virtually all virus was extracellular. Thereafter infectivity declined with a half life of approximately 12–14 hours at 37°C. Inactivation was not retarded by cystine 0·01%, glutamine 0·3%, calf serum 10%, or by anaerobic conditions. A typical virus preparation obtained by this technique had a titre of 2×10^9 PFU per ml. and contained 10^{12} PFU of poliovirus per gramme of protein.

An essential prerequisite for success with this high density suspended cell technique is healthy cells and a single cycle of infection. Cells usually yielded 200 PFU but about 20% of cell batches yielded only 50 PFU; this was presumably due to "unhealthy" cells, but attempts to elucidate the factors involved were unsuccessful. Normally cell suspensions were held for 2 hours before infection, during preparation. If this was prolonged to 6 hours at 20°C. the yield fell 3-fold, and 6-fold if held for the same time at 37°C. This fall in yield could be partially reversed by additional glucose.

[DARNELL *et al.* (this *Bulletin*, 1960, v. 35, 90) using cell densities at least 20 times more dilute than those in the above experiments found that the nutritional requirements for poliovirus production by HeLa cells increased on dilution of the cells. See also WESTWOOD *et al., ib.d.*, 937.] *A. J. Beale*

SCHAFFER, F. L., MOORE Helen F. & SCHWERDT, C. E. **Base Composition of the Ribonucleic Acids of the Three Types of Poliovirus.** *Virology*. New York. 1960, Apr., v. 10, No. 4, 530–37. [22 refs.]

The base composition of a representative strain of each of the 3 types of poliovirus was determined and compared with that of host cells (FL strain of human amnion cells and HeLa cells). It was found that there was no significant difference in base composition of the 3 types but that these were substantially different from host cells. Thus, assuming a total of 4 units, the composition of poliovirus and FL cells respectively was guanine 0·96, 1·28; adenine 1·14, 0·86; uracil 1·01, 0·68; cytosine 0·88, 1·18. The authors point out that the virus RNA may be more similar to some special RNA-containing component of the cell. The methods developed are presented together with the results of a turnip yellow mosaic virus control in detail. *A. J. Beale*

HODES, H. L., ZEPP, Helen D. & AINBENDER, E. **A Physical Property as a Virus Marker. Differences in Avidity of Cellulose Resin for Virulent (Mahoney) and Attenuated (LSc,2ab) Strain of Type 1 Poliovirus.** *Virology*. New York. 1960, May, v. 11, No. 1, 306–8, 1 fig.

Another marker characteristic (elution: E) of poliovirus is described. Some strains of poliovirus are virtually completely adsorbed onto a DEAE (diethylaminoethyl) cellulose column from 0·02 M phosphate buffer at *p*H 7·1 under standard conditions, whereas others are not. Thus the Mahoney strain is not adsorbed, 94% appearing in a 0·02 M phosphate buffer "eluant", while the LSc 2ab attenuated strain selected by Sabin was adsorbed, only 0·8% being recovered from the column under the same conditions. A sample taken from a child who had been fed the Sabin strain was similarly tested and 7 and 10% was recovered in 2 experiments. This strain also showed slightly increased neurovirulence for monkeys according to Sabin, so the authors wonder if the E character and neurovirulence may be associated. *A. J. Beale*

KIRSCHSTEIN, Ruth, BARON, S., BORMAN, G. S., MURRAY, R., PERKINS, F. T. & HOTTLE, G. **Neurovirulence of Attenuated Type 1 Poliovirus Vaccine Strains after Intramuscular Inoculation of Rhesus Monkeys.** *Virology*. New York. 1960, May, v. 11, No. 1, 300–302.

The attenuated strains of type 1 poliovirus of KOPROWSKI (Chat, pool 13, titre $10^{7·2}$ PFU/ml.), LEDERLE (lot

lumber 7–1231–166, titre $10^{7.9}$ PFU/ml.) and SABIN LSc 2ab, titre $10^{7.7}$ PFU/ml.) were tested for neuro-irulence for rhesus monkeys by the intramuscular route. t was found that animals were paralysed by the Kop-owski and Lederle strains in doses of 1 or 10 ml. into he gluteus. Thus 2/2 and 5/9 were paralysed by a ml. dose of the Koprowski and Lederle strains respect-vely. Histological lesions appeared in all the paralysed nimals and in many that were not paralysed. The esions were distributed widely in the CNS. By contrast abin's strains caused no paralysis even in a 10 ml. dose, ut 8 out of 13 animals given 10 or 1 ml. into the luteus developed localized lumbar cord lesions, in 1 preading to involve the cervical cord and brain stem. similar difference between the Sabin strain on the one and and the Koprowski and Lederle strains on the other as observed after inoculation into the deltoid, although nly histological lesions were observed. The route of pread is not known. The authors state that viraemia oes sometimes occur after intramuscular inoculation of ese strains but also that the lesions with Sabin's strains re confined to the CNS site innervating the area inocu-ted. *A. J. Beale*

AETTIG, H. & GODGLÜCK, G. Provokation einer Infektion durch Schutzimpfung. V. Mitteilung: Provokation nach experimenteller Infektion mit mäuseadaptiertem Poliomyelitisvirus. [**Provocation of an Infection by Vaccination. 5th Communication: Provocation following Experimental Infection with Mouse-Adapted Poliomyelitis Virus**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 1, 93–112, 6 figs. [28 refs.]

In experiments carried out on more than 1,000 mice fected intracerebrally with the MEF 207 strain of type poliomyelitis virus it was found that subcutaneous fection with a single dose of commercial poliomyelitis ccine given 4–7 days after infection caused a significant duction in the survival time as compared with control nimals which were infected but did not receive vaccine. similar provocation of the virus infection was also oted in further experiments with vaccine consisting of a spension of *Salmonella typhi-murium* inactivated with at and phenol. No provocation was observed in 284 ice which were previously treated with poliomyelitis ccine in order to produce a certain degree of immunity ee also this *Bulletin*, 1959, v. 34, 1282, *bis*; 1960, 35, 0]. *D. J. Bauer*

DAH, J. D., BJOTVEDT, G. & VAINIO, T. **Protection against Liver Injury due to Murine Hepatitis Virus.** [Correspondence.] *Nature.* 1960, Aug. 6, v. 187, 507–8.

It has previously been found that antihistamines confer otection against liver injury (GALLAGHER *et al., J. Path. Bact.*, 1956, v. 72, 193), and in the present work an vestigation has been made of the effect of Benadryl in e liver injury caused in mice by infection with the HV3 strain of murine hepatitis virus. 26 of 61 mice infected intraperitoneally [dose of virus not stated] and given Benadryl each day subcutaneously in a dose of 100 mgm. per kgm. were still alive after 7 days, compared with 11 of 68 controls which were similarly infected but received no treatment. The malic dehydrogenase activity of the serum (an index of liver damage) was also lower in the treated animals. There was no difference in the titres of virus in the liver in the treated and control groups, and the effect of the drug was therefore to prevent liver necrosis without affecting the multiplication of virus. Benadryl also exerted a protective effect in organ cultures of mouse liver made by the technique of BANG and WARWICK (*Virology*, 1959, v. 9, 715). *D. J. Bauer*

TRANS. ROY. SOC. TROP. MED. & HYG. 1960, Mar., v. 54, No. 2, 89–129, 3 figs. [Numerous refs.] Discussion 130–34. **Symposium on the Evolution of Arborvirus Diseases.**

Those who contemplate the rapidly increasing number of viruses isolated from insects sometimes ask where this accumulation of viruses, most of them not associated with a disease, is leading us. The Symposium now abstracted goes a long way towards supplying an answer.

The first of the three main papers is by C. D. DARLINGTON (Botany School, Oxford) on the *Origin and Evolution of Viruses* (pp. 90–96). Professor Darlington treats his subject on broad biological lines, drawing his instances from the whole field of virology and relating evolutionary changes in viruses to their genetic behaviour. He discusses virus-vector relationships and the adaptations they lead to in both viruses and hosts.

The second paper, by P. F. MATTINGLY (British Museum, Natural History), on *Ecological Aspects of the Evolution of Mosquito-borne Virus Diseases* (pp. 97–112), contains a very large amount of information from the author's own work and other people's. An abstract cannot do justice to it. The author stresses the importance of studying not only the forms of hosts and vectors, but their habits and habitats as well, and especially the vegetation with which they are associated—the entire biocenose. BAKER [*Trop. Dis. Bull.*, 1944, v. 41, 196] first suggested that arboviruses originated in their arthropod hosts, either *de novo* or by degeneration of more complex organisms. Probably acarines and mosquitos " evolved together with warm-blooded vertebrates and angiospermous plants, during the latter part of the Mesozoic, their evolution being closely integrated with that of their vertebrate hosts and vegetational habitat ". Both the arthropod-borne viruses and the rickettsias must have assumed their present forms in connexion with the evolution of blood-sucking habits on the part of their arthropod vectors.

Among mosquitos, viruses have been obtained from very few anophelines, and then from kinds which breed in epiphytic bromeliads and are therefore associated with the forest canopy. Most virus vectors are culicines, extensive feeders on birds; but the author is very wary about concluding that arbor viruses may have originated in birds; he considers that there is far too little evidence to justify such an assumption.

The evolution of a virus must have been related to its epidemiology. Promiscuously feeding arthropods are unlikely to favour the evolution of a stable virus reservoir, but may well encourage new transmission cycles. Cross immunity between related viruses must also play a part. These and other factors are discussed at some length in respect of the following Group B viruses: (a) West Nile, St. Louis, Japanese B, Murray valley, Ilhéus and Ntaya; (b) yellow fever, Uganda S and SAH 336; (c) dengue-1 (Hawaiian) and dengue-2 (New Guinea) (d) Russian spring-summer, louping ill, Omsk and Crimean haemorrhagic, central European, Kyasanur and TP21; and (e) a miscellaneous group comprising Zika, Spondweni, Wesselsbron and bat salivary gland virus.

"The most striking feature of the geography of the Group B viruses is the exclusion of *Aedes*-borne viruses from the northern subtropics", where the important vectors are *Culex*. Further north, *Culex* in turn gives way to the tick as the commonest vector.

Some evidence is presented that the West Nile virus is the most primitive of the group, pointing to the general area embracing Egypt and north-west India as the possible original home of the Group B viruses.

The author's careful argument suggests, with more clarity than one might have expected from the complexity of the subject, a probable line along which evolution in this group of viruses may have proceeded.

C. E. Gordon Smith (London School of Hygiene and Tropical Medicine) contributed the third paper, on *Factors in the Past and Future Evolution of the Arboviruses* (pp. 113–129). After a brief description of the geographical distribution of the Group A and Group B arboviruses, the author discusses their relation to human disease, quoting Sabin to the effect that of approximately 74 known arthropod-borne viruses, 50 are still "in search of a disease" [this *Bulletin*, 1960, v. 35, 95], but antibodies to 14 of these suggest that they do at least infect man. Some of the viruses not known to cause human disease may represent stages in arborvirus evolution, from a first stage in which only the arthropods are infected, through stages in which reservoir hosts other than man are involved, to those in the transmission cycle of which man plays a part, and finally to the specifically human viruses, kept going by arthropod transmission from man to man, or even by direct transmission without the intervention of an arthropod vector.

In nature, arboviruses are maintained by mechanisms of great complexity, involving delicate quantitative balances between the elements of each biocenose. A factor in the mechanism is the susceptibility of host populations, which may determine the duration of a viraemic phase in which transmission is possible. Insect behaviour, as Mattingly stresses, and also the behaviour of vertebrate hosts including man, profoundly affect transmission cycles. Man's use of chemoprophylaxis and chemotherapy has affected other diseases; insecticides and older ecological operations, such as irrigation, have altered the epidemiology of virus diseases, not always in the manner expected.

The viruses, varying in antigenic structure, in the hosts that they can infect, and in virulence, themselves affect their own epidemiological behaviour.

Available data about arboviruses are often difficult to interpret. The close serological similarity of related viruses, especially in Group B; the difficulty of knowing whether a virus found in an arthropod was multiplying or merely mechanically picked up; the choice of experimental animals and culture media; the risks of "laboratory pick-up"—these are all problems which arise with nearly every isolation. To incriminate an arthropod as a vector, one must isolate a virus from wild-caught insects; one must be sure that natural vertebrate hosts can carry the virus in their blood for long enough; one must be sure that quantitative considerations are consistent with adequate transmission; and finally one must successfully demonstrate transmission—itself a task beset with difficulties, some of which the author discusses.

Like the second paper, this article by Gordon Smith contains so much information that it is difficult to abstract fairly. It ends with a short discussion of some of the outstanding problems in the field of arborvirus evolution and behaviour which await solution.

In the discussion which follows these papers (pp. 130–134), C. H. Andrewes offers comments on each of them, and raises the question whether ticks may not have preceded culicines in the evolution of arboviruses D. S. Bertram describes experiments with Semliki forest virus indicating that a mosquito may be able to transmit mechanically before enough time has passed to allow virus multiplication in it. He also suggests that ticks may have been vectors before mosquitos entered the field. J. S. Porterfield considers that antigenic modifications of evolutionary significance may establish themselves in quite short times. M. G. R. Varma points out that the vector of Kyasanur forest virus seems to be *Haemaphysalis spinigera* and not *Ixodes* which is the vector of other members of the RSS group. There is some evidence that mosquito-borne viruses can multiply in ticks, but not vice versa. P. B. Stones describes isolation of Semliki forest virus from a male *Eretmopodites* mosquito. P. H. A. Sneath wonders whether the genetic material of the arboviruses may not have originated in the genetic material of their hosts.

Short comments by the three principal contributors bring to an end this most informative and stimulating symposium. *E. T. C. Spooner*

Shah, K. V., Johnson, H. N., Rao, T. R., Rajagopalan, P. K. & Lamba, B. S. **Isolation of Five Strains of Sindbis Virus in India.** *Indian J. Med. Res.* 1960, May, v. 48, No. 3, 300–308.

Strains of virus were isolated:— (1) From a pool of 3 spleens of white wagtails (*Motacilla alba*) collected in October from near Poona. 52 of this species were tested. Wagtails had a 35% infection rate with haemoproteus. (2) From the spleens of 2 hill mynas (*Gracula religiosa*) collected in December from near Cochin. Both had haemoproteus, filaria and leucocytozoon or trypanosomes. (3) From a pool of culicines (17 *Culex vishnui*, 12 *C. khazani*, 4 *C. mimulus*, 2 *C. bietaeniorhynchus*, 15 *Mochthogenes*) caught in December in outdoor resting places along the Beniholi river. (4) From a pool of 300 *Bdellonyssus bursa* mites from domestic chickens in December at Rogihosalli on the Sirsi-Kumta road.

The viruses were isolated by inoculation of the field specimen into young male mice: the brains of sick mice were passaged to infant mice. 4 of the 5 strains caused 100% mortality in infant mice in the 2nd or 3rd passage. The mite strain caused irregular disease in mice until the 10th passage. Mice under 3 days old were highly susceptible but by 1 week of age susceptibility fell sharply and adult mice usually remained healthy. All the strains grew well in 5–7-day chick embryos. The *Culex* strain was easily adapted to chick embryo tissue culture causing cytopathic effects and plaque-formation. Two strains were found to circulate in chicks 1–7 days old, 3–4 days after inoculation.

Macaca mulatta were inoculated with 3 strains intracerebrally or subcutaneously: one strain caused viraemia but none fever or symptoms. Two of the strains were shown by CASALS to be identical or closely related to Sindbis virus and the other strains by cross-neutralization tests were shown to resemble the identified strain closely.

A survey for neutralizing antibody testing undiluted serum against the mite strain was made on human sera from 2 areas in Bombay and 1 in Mysore: 4 of 43 sera from children under 15 years and 5 of 164 from persons over 15 years were positive. None of 64 sera from Jamshedpur, to which fresh serum was not added, were found positive, human infections thus seem to be uncommon in India. No antibody was demonstrated in 57 *M. mulatta* from North India. 1 of 8 horses which had a paralytic illness had antibody as did 1 of 20 crows from the Poona area. None of 19 fowls from the Poona area had antibody.

This is the first demonstration of a group A arbovirus in India and also the first isolation of Sindbis virus from a migratory bird—the white wagtail. The isolation from mites was probably from the blood they contained from a recent feed on a viraemic fowl.

C. E. Gordon Smith

SULKIN, S. E., ALLEN, R. & SIMS, Ruth. **Lipotropism in Pathogenesis of Encephalitis Viruses in Insectivorous Bats.** *Virology*. New York. 1960, May, v. 11, No. 1, 302–6.

IMMUNITY

BACT. REVIEWS. 1960, Mar., v. 24, No. 1, 1–200, illustrated. [Numerous refs.] **The 1959 Fort Detrick Symposium on Nonspecific Resistance to Infection held at Hood College, Frederick, Maryland, 16 and 17 September 1959.**

The programme for this Symposium, sponsored by the U.S. Army Chemical Corps, was drawn up by the Conference Chairman, Dr. C. M. MACLEOD (University of Pennsylvania), Drs. I. L. BENNETT Jr. and L. E. CLUFF (Johns Hopkins), Dr. R. J. DUBOS (Rockefeller Institute) and Dr. H. N. GLASSMAN (Fort Detrick).

The Symposium opened with a paper by H. HARRIS (Oxford, England) on *Mobilization of defensive cells in inflammatory tissue* (pp. 3–15). Recalling that very little on the subjects of leucocyte emigration and chemotaxis had been added to the classical work of METCHNIKOFF, he said that the present position is that there is no evidence that chemotaxis is involved in the emigration of polymorphonuclear leucocytes through vessel walls; once the cells are out in the tissues their movement may be influenced by chemotactic substances, but there is no acceptable evidence that chemotactic substances are produced by the tissues themselves. A wide range of microorganisms produce chemotactic substances, but the identification of these substances has not been achieved; there are some indications, but no rigid proof, that they are polysaccharide in type. Harris discussed also the emigration and chemotaxis of monocytes (demonstrated by the dark-ground trace technique), and the mechanisms of eosinophil and lymphocyte accumulation.

I. L. BENNETT JR. and A. NICASTRI (Baltimore) in *Fever as a mechanism of resistance* (pp. 16–34) gave a review of the literature on the effects of fever on hypersensitivity, antibody formation, bacterial infections and some viral infections. There appears to be very little good evidence that fever does act as a mechanism of resistance, but there are many interesting and suggestive phenomena which require further study.

The *Influence of irradiation on resistance to infection* (pp. 35–40) was discussed by B. BENACERRAF (New York). The several factors in the anti-infectious mechanism are dealt with in turn—antibody response, polymorphonuclear leucocyte circulation, bactericidal power of the serum and the reticulo-endothelial system. [This condensed paper is full of facts, but is difficult to summarize as it lacks headings and sub-headings; reference should be made to the original by those interested.]

W. BARRY WOOD JR. (Baltimore) reviewed the present position of *Phagocytosis, with particular reference to encapsulated bacteria* (pp. 41–49). ZINSSER's immunological dictum that fully encapsulated bacteria could not be phagocytosed except in the presence of opsonins is not tenable; it is true of *in vitro* experiments, but not of the situation in the living host. When a mixture of encapsulated bacteria and phagocytes is placed, not on a glass slide, but on the surface of freshly excised tissue (or even on such an inert surface as that of moistened filter paper), phagocytosis ensues although antibodies are not involved; because the immovable surface of the tissue is used in the process, the resulting reaction has been called "surface phagocytosis". When the phenomenon occurs in a dense exudate (where the leucocytes are packed closely together) it has been called "intracellular surface phagocytosis". Recently surface phagocytosis has been studied in infections caused by group A haemolytic streptococci. There appears to be a significant correlation between virulence and susceptibility to surface phagocytosis both *in vitro* and *in vivo*.

Host mechanisms which act to remove bacteria from

the blood stream (pp. 50–66) were discussed by D. E. ROGERS (Nashville, Tennessee). Tissues active in the trapping of micro-organisms probably include the reticulo-endothelial system, the circulating leucocytes, and leucocytes sequestered in various capillary beds. There are indications that this removal system (which has immense reserve power) can adapt variably, depending on the nature or the duration of the bacteriaemic stimulus. Past experience with the invading bacteria can greatly enhance the removal, and possibly the destruction, of blood-borne bacteria, but is not a pre-requisite for effective blood stream clearance. The outcome of bacteriaemia appears to depend upon the ability of fixed and circulating phagocytic cells to retain and destroy ingested micro-organisms. There are increasing indications that this intracellular phase can be altered in favour of the parasite by many states, *e.g.* starvation, known empirically to affect host resistance.

A lengthy review of *Cellular Immunity* (pp. 67–95) was given by S. S. ELBERG (Berkeley, California). After dealing with the interaction between parasite and phagocytic cell, he describes experiments on the response of mononuclear phagocytes to *Mycobacterium tuberculosis* and *Brucella melitensis*. He shows that (a) normal monocytes are lysed by certain ingested virulent bacteria but not by avirulent ones, and that "immune" monocytes are not "lysed" by homologous parasites: (b) "immune" monocytes can support growth of the homologous parasite temporarily but it then decreases and stops: (c) the immunity in its quantitative expression suggests that the parasite does actually persist as an elementary particle: (d) the immunity is group specific: (e) by a change in the identity of the serum component of the cell culture system, intraphagocytic multiplication can be stopped or induced: and (f) the stubborn persistence of the concept of "infection immunity" in tuberculosis, brucellosis and other infectious diseases is strongly supported by data from so-called "superinfection type" experiments. [There is a list of 109 references.]

Z. A. COHN (New York) discussed *The relation of cell metabolism to infection with rickettsial and bacterial agents* (pp. 96–105). In dealing with these two specific examples in which metabolic changes in either host cell or parasite result in alterations in activity, the author presents evidence that suggests that the metabolic integrity of the rickettsiae plays an important role in the invasion of host cells, whereas on the other hand the leucocyte's metabolism is the important thing in the ingestion of bacteria. Among other things, it was found that both the ingestion of particles and the presence of minute quantities of a lipopolysaccharide endotoxin influence the metabolism and phagocytic activity of the polymorphonuclear leucocyte. Whether or not it will be possible to alter the bactericidal properties of the leucocytic cytoplasm is an important field for future investigation.

Antibacterial systems of serum in relation to non-specific immuniy to infection (pp. 106–114) were dealt with by D. ROWLEY (Adelaide). After discussing the contribution to the over-all immunity of the host made by each of the known antibacterial systems of serum, *viz.* the complement-properdin system, lysozyme and beta-lysins, he describes experimental work to study the sequence of events which follow intraperitoneal injection of bacteria into mice. Describing the bactericidal effects due to the macrophages, he shows that the rate of phagocytosis is dependent on the presence of opsonic factors; virulent strains of bacteria are not phagocytosed at all unless they are presensitized, whereas avirulent strains are removed from the peritoneum quite rapidly even without presensitization, presumably because sufficient opsonic factors are available in the peritoneal fluids for this purpose. The problem of defining the determinants of species immunity seems to defy explanation on the basis of O-specific antibody, and the author wonders if these opsonic factors may provide the explanation.

A group of workers, R. A. GOOD, R. A. BRIDGES and R. M. CONDIE, from Minneapolis, Minn., discussed *Host-parasite relationships in patients with dysproteinemias* (pp. 115–132). At first sight it would appear that agammaglobulinaemic patients handle virus infections well and bacterial infections poorly, but this is not strictly true, because, for example, such patients are inordinately vulnerable to infection with the virus of homologous serum hepatitis. Mention is made of delayed allergy and tuberculosis, collagen diseases and immunoelectrophoretic studies in patients with agammaglobulinaemia. Host response is also discussed with reference to multiple myeloma, macroglobulinaemia, dysgammaglobulinaemia and Hodgkin's disease. [There are 198 references.]

Antimicrobial factors in tissues and phagocytic cells (pp. 133–140) were considered by J. G. HIRSCH (New York). He deals with certain tissue and cell substances potentially toxic for micro-organisms, stressing biochemical classification of these agents and speculating on the possibility of their antimicrobial activity *in vivo*. Of such substances in normal tissues he mentions oxygen, carbon dioxide, fatty acids, lactic acid, lipids, porphyrins, proteins (*e.g.* lysozyme), peptides, histones, globin, and spermine. Substances in phagocytic cells are acids (lactic acid), long-chain fatty acids, lysozyme, phagocytin and histones. There may be additional antimicrobial factors in inflamed or necrotic tissues, but also factors present in normal tissues may be released from a bound state (as is phagocytin) when the tissues become inflamed.

H. S. GINSBERG (Cleveland, Ohio) read a paper on *Serum and tissue inhibitors of virus* (pp. 141–150). Inhibitors from the tissues are mainly mucoproteins, glycoproteins, mucopolysaccharides and lipoproteins; except for the last, they tend to inhibit haemagglutination but not infectivity. The inhibitors in the serum may be heat-stable (mucoprotein or lipid), or heat-labile; the latter are associated with the properdin system and the paper ends with a discussion on the viruses which are (a) inactivated, (b) probably inactivated and (c) not inactivated, by the properdin system. Of all the inhibitors, there is as yet no evidence that any one of them is responsible for resistance to infection; properdin and its cofactors may play a role in non-specific resistance to infection but this is still to be proved.

Viral interference: some consideration of basic mechanisms and their potential relationship to host resistance (pp. 151–166) was the subject of a paper by R. R. WAGNER (Baltimore, Maryland). After dealing

with the three phenomena of bacteriophage "interference", *viz.* resistance to lysis from without, immunity of lysogenic bacteria, and the mutual exclusion and depressor effect, he goes on to discuss interference between animal viruses: (a) the site of viral interference, (b) the role of virus nucleic acids in interference, and (c) interferons. He deals in particular with his own work on the inhibition in monolayer cultures of chick embryo fibroblasts of eastern equine encephalomyelitis virus by allantoic fluid infected with the WS strain of influenza A virus. Comparing this work with that of others (*e.g.* ISAACS, HENLE, etc.) he advances a theory that a persistent low grade infection can be established in cell cultures by virtue of cyclic production of both virus and interfering substance in response to viral infection.

D. W. HENDERSON (Porton, England), discussing some recent work on *Bacterial Interference* (pp. 167–176), describes experimental infection of guineapigs and mice with *Brucella suis, Bacillus anthracis, Pasteurella pestis* and *Mycobacterium tuberculosis*. In guineapigs in certain circumstances a pre-existing infection can induce a high degree of non-specific resistance to a second and wholly unrelated infection, whereas under other conditions, with the same organisms, no trace of resistance is observed. Mice react quite differently to infection with *Br. suis* and *B. anthracis*: the essential difference is that in infections with these organisms in the guineapig lymphoid and lymphatic invasion is dominant, whereas in the mouse it is minimal or absent. If infectious agents could be found that would choose the respiratory lymphatic pathway as the portal of entry, would non-specific resistance manifest itself in the mouse as it does in the guineapig?

Hormones and host resistance to infection (pp. 177–185) was read by E. H. KASS (Boston, Mass.). Although little can be said at present of the influence of hormones on resistance to infection, there is reason to believe from studies of the influence of thyroid and adrenocortical hormones that the physiological effects of infection can be differentiated from the resistance mechanisms that inhibit bacterial multiplication. Sometimes the toxic effect of an infection is such that it overshadows the capacity of the host to restrain the multiplication of infectious agents in host tissues. Evidence is presented which indicates that hormonal changes accompanying pregnancy act as predisposing factors in increasing the incidence of bacteriuria during pregnancy and in sensitizing the uterus to endotoxin.

H. A. SCHNEIDER (New York), in a philosophical paper, discusses *Nutritional factors in host resistance* (pp. 186–191). Reference is made to the work of DUBOS and SCHAEDLER on protein nutrition [see this *Bulletin*, 1958, v. 33, 1195; 1960, v. 35, 522 *bis*], and much of the paper discusses "mean survival time" versus "survivorship", but after a discourse on semantics, parametrics and panmictic breeding (without very much mention of nutritional factors) he concludes: "Is it any wonder that progress has been slow?"

Genetic effects in nonspecific resistance to infectious disease (pp. 192–200), the final paper, was read by J. W. GOWEN (Ames, Iowa). This paper considers non-specific resistance to infectious disease largely on the basis of evidence from one disease, mouse typhoid as initiated by *Salmonella typhi-murium* 11C in one host species, *Mus musculus*, under a limited number of environmental conditions. The subject is discussed under the headings: host constitution and resistance, non-specific host resistance to infectious disease, pathogen specificity and specificity of other factors in infectious disease. By means of a plaster model the author demonstrates the associations of the genotypes of host and pathogen in governing the severity of a disease. *D. A. Cannon*

PARISH, H. J. **Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment.**

This book was reviewed on p. 1070.

EDELMAN, G. M., HEREMANS, J. F., HEREMANS, M. T. & KUNKEL, H. G. **Immunological Studies of Human γ-Globulin. Relation of the Precipitin Lines of Whole γ-Globulin to those of the Fragments produced by Papain.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 203–23, 11 figs. [21 refs.]

SMITH, C. W., METZGER, J. F., ZACKS, S. I. & KASE, Alice. **Immune Electron Microscopy.** *Proc. Soc. Exper. Biol. & Med.* 1960, June, v. 104, No. 2, 336–8, 2 figs.

"A method is described by which immune systems can be studied at subcellular level with the electron microscope, using a ferritin-antibody conjugate. A conjugated immune serum to *Staphylococcus aureus* was applied to homologous organisms, embedded in methacrylate with uranium and thin sections cut. An antigen-antibody reaction was detected by attachment of the ferritin molecule in the capsule-like material. Use of formalin in primary fixation for electron microscopy as well as non-specific immunofluorescence is discussed."

LIEBERMAN, Rose, DOUGLAS, J. O. A. & MANTEL, N. **Production in Mice of Ascitic Fluid containing Antibodies induced by *Staphylococcus*- or *Salmonella*-Adjuvant Mixtures.** *J. Immunology.* 1960, May, v. 84, No. 5, 514–29, 4 figs.

Antigenic material derived from *Staphylococcus aureus*, Strain 18 or Strain 2 or *Salmonella enteritidis* was mixed with equal parts of incomplete Freund's adjuvant (100 ml. of a mixture of 85 ml. Bayol F (Esso, Standard Oil Co., N.J.) and 15 ml. Arlacel A (Atlas Powder, New Castle, Delaware)) and injected intraperitoneally into mice as 2–3 doses of 0·4–0·5 ml. at 3–7 days' intervals. High yields of ascitic fluid were elicited by these procedures and booster doses further increased the yield. The gamma globulin average level for ascitic fluid was 0·86 gm./100 ml. and constituted about 22% of the total protein. Protein levels for ascitic fluid were about 70% that for serum. With *Staph. aureus*

18 in paraffin oil adjuvant the agglutinin titres of the ascitic fluid showed an early rise of 1 : 500–1 : 1,000 which was sustained for a period of 4–5 months and comparable titres were found in the limited numbers of sera tested. Ascitic fluid from mice immunized against *Salm. enteritidis* afforded significant protection of mice against homologous challenge, the comparable doses of ascitic fluid and serum in this respect was 0·005 ml. to 0·01 ml. In the ascitic mice the peritoneal granulomas and the peripheral lymph nodes contained large numbers of plasma cells. The early produced ascitic fluids were significantly more cellular than the later fluids and whereas the former contained mainly polynuclear cells the latter exudates contained cells of which 90% were mononuclears. The ascitic fluid obtained by the procedures described was a potential source of protective and agglutinating antibodies, viable leucocytes and gamma globulin.

[It is to be noted that the authors use the term *Salmonella enteriditis* to indicate *Salmonella enteritidis*.

H. J. Bensted

NOSSAL, G. J. V. **Studies on the Transfer of Antibody-Producing Capacity. II. The Serial Transfer of Antibody-Producing Cells.** *Immunology*. Oxford. 1960, Apr., v. 3, No. 2, 109–16, 4 figs. [14 refs.]

In a previous paper the author [this *Bulletin*, 1960, v. 35, 96] showed that spleen cells from a rat primarily immunized against a *Salmonella* flagellar antigen could be secondarily stimulated *in vitro* to form antibody on transfer to homologous newborn rats. The present paper reports the continuation of this work in which serial transfer of the spleen cells from host rats, killed 2 weeks after receiving the intraperitoneal injection of treated spleen cells, was repeated up to 7 times. That is to say, rats were first immunized with a *Salmonella* flagellar antigen. 4–8 weeks later they were killed. The spleens were then removed for the preparation of spleen cell suspensions which were first incubated at 37°C. with a suspension of the flagellar antigen used for the original immunization before being injected intraperitoneally into infant rats less than 48 hours old. 2 weeks later the serial transfer experiments were started, so that the host rats were immunologically immature when they were killed for the spleen cell preparations, some of which were exposed *in vitro* to the antigen for further stimulation and others were not so treated. It was found that where spleen cells were not stimulated antigenetically by *in vitro* treatment the formation of antibody was relatively poor and passage was not successful after 2 or 3 transfers, but with the antigenic stimulation much more antibody was produced and passage was successful up to 5 passages.

Immunization of donor animals with two unrelated antigens, with later *in vitro* stimulation with only one of these antigens, resulted in the development of far more antibody to the antigen used for this stimulation than the other.

H. J. Bensted

TAYLOR, E. M. & MOLONEY, P. J. **Assay of Diphtheria and Tetanus Antitoxins in Small Volumes of Blood.** *Canadian J. Pub. Health.* 1960, Apr., v. 51, No. 4, 135–8.

GOODMAN, J. W. & KABAT, E. A. **Immunochemical Studies on Cross-Reactions of Antipneumococcal Sera. I. Cross-Reactions of Types II and XX Antipneumococcal Sera with Dextrans and of Type II Antipneumococcal Serum with Glycogen and Friedländer Type B Polysaccharide.** *J. Immunology*. 1960, Apr., v. 84, No. 4, 333–46, 4 figs. [40 refs.] **II. Cross-Reactions of Types IX and XII Antipneumococcal Sera with Dextrans.** *Ibid.*, 347–57, 3 figs. [25 refs.]

I. A quantitative immunochemical investigation of the cross-reactions of dextrans with types II and XX antipneumococcal sera (designated anti-SII and anti-SXX) as well as the cross-reactions of type II antiserum with glycogen and Friedländer Type B polysaccharide is reported. In general dextrans with 70% or more α-1,6 linkages are equally efficient in precipitating the cross-reacting antibody present in anti-SII and anti-SXX; precipitation efficiency declines with decreasing proportions of 1,6 linkages below 70%. Oligosaccharides of the isomaltose series are the best inhibitors of the cross-reactions of dextrans with anti-SII or anti-SXX and also of glycogen and anti-SII. Glucuronic acid residues may be involved in the cross-reaction of Friedländer Type B polysaccharide with a fraction of anti-SII which is independent, in part, from the fraction cross-reacting with dextrans.

II. *N*-acetylglucosamine and glucuronic acid may be involved in the specificity of the cross-reacting fraction of type IX antipneumococcal sera with a variety of dextrans. Similarly the specificity of the cross-reactions of a fraction of type XII antipneumococcal sera with dextrans may involve *n*-acetylglucosamine.

[These papers contain a considerable amount of complex data derived from quantitative precipitin studies performed with homologous and heterologous polysaccharides and the various antipneumococcal sera. Such data cannot be adequately reviewed in a short summary and interested readers should consult the original papers.]

H. Gooder

FRIEDMAN, H. & GABY, W. L. **Immunologic Unresponsiveness to *Shigella* Antigens in Chickens.** *J. Immunology*. 1960, May, v. 84, No. 5, 441–8, 3 figs. [30 refs.]

Partial acquired immunological unresponsiveness to bacillary suspensions or a soluble antigen derivative of *Shigella paradysenteriae* (presumably Flexner bacilli) was demonstrated in chickens by injecting such antigens into embryos and young chicks of the ages of 15-day-old eggs to 2-day-old chicks. It would appear that the results are not completely compatible with the phenomena of either acquired immunological tolerance or with those of immunological paralysis. There is, however, a

close similarity between the conditions needed to suppress agglutinin response by embryonic or neonatal injection and that of the unresponsiveness following large injections of soluble serum proteins. The concentration of the antigen injected influenced the degree of the unresponsiveness and injections into the chorioallantoic vein were far more effective in this respect than intramuscular or yolk-sac injections. Normally the test and control chickens were challenged with an intramuscular dose of the *Shigella* vaccine at the age of 100 days; when treated chicks were challenged at 150 days the antibody response was similar to that of the untreated controls. The response to heterologous antigens, as tested by the injection of red blood cells in treated birds and untreated controls at 50 and 100 days after hatching, appeared to be unimpaired. ^{14}C-labelled antigen in the same concentration as used in the other experiments was injected into embryos. There was no detectable radioactivity in the sera, spleens or other tissues of these chicks after one week although agglutinin formation in similarly treated chicks was suppressed when challenged at 50 days. *H. J. Bensted*

PELS LEUSDEN, F. & MÜLLER-RUCHHOLTZ, W. Eigenhemmungen infolge von Autoantikörpern (?). **[The Possible Role of Auto-Antibodies in Complement Deviation]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Dec., v. 118, No. 6, 466–81. [15 refs.]

The authors have set out to analyse the factors responsible for anti-complementary action in sera examined for activity in promoting complement fixation in the presence of an appropriate antigen. The main conclusions reached are that two mechanisms come into play: the first of these is complement adsorption such as has been shown to occur with yeast, *Escherichia* or *Serratia*. In this form of adsorption it is the C3 element in complement which is adsorbed and this element is heat stable. In antigen-antibody reaction the other fractions of complement C2, C4 and C1 are involved and these are thermolabile. As a consequence a serum saturated with complement to the limit of powers of adsorption will not, when heated, have any of its capacity for complement adsorption restored, whereas the anti-complementary effect due to an antigen-antibody reaction will, on heating, be restored on account of the destruction of the labile complement components. It will, on heating at 56°C., be found to be as capable of taking up complement as previously. It is suggested that by such observations the distinction between the anti-complementary action due to adsorption on the one hand and due to the action of auto-antibodies reacting with components of the serum on the other hand may be differentiated.

A table of the results is presented with 13 anti-complementary samples selected from a much larger number of sera under examination by the Wassermann test. This shows that in some of these the capacity for neutralizing complement is restored by heating after saturation, whereas with others it is not.

J. W. McLeod

RAPPAPORT, B. Z. **Antigen-Antibody Reactions in Allergic Human Tissues. I. Preparation and Use of Fluorescein-Conjugated Reagins for Staining the Reaction Sites.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 55–64, 12 figs. on 2 pls. [15 refs.]

SALVIN, S. B. & SMITH, R. F., with the technical assistance of Jane NISHIO & L. A. CHITWOOD. **Delayed Hypersensitivity and the Anamnestic Response.** *J. Immunology.* 1960, May, v. 84, No. 5, 449–57, 3 figs. [18 refs.]

Using diphtheria toxoid and a crystalline preparation of egg albumin as antigens, the authors studied the relationship of the size of the dose to the development of (a) delayed response of the skin to a second injection of the same antigen given intradermally, (b) the development of circulating antibody and (c) the Arthus phenomenon, *i.e.* the development of a rapid and severe local reaction to a second injection of the same protein.

With injections of 0·1 Lf of toxoid or 0·5 μgm. of egg albumin it was possible to get delayed skin reactions on intradermal testing without either the development of detectable circulating antibody or skin reaction of the Arthus type within 5 or 6 weeks.

The influence of the time at which a secondary sensitizing dose was administered on the development of circulating antibody and an Arthus reaction was also studied and it was found that the most rapid response followed second injections 15–16 days after the first; that is, at the moment of maximal delayed skin sensitivity dependent on the first dose.

X-irradiation of guineapigs (200 r) did not affect the development of the anamnestic response, whether administered prior to the first or second injection of antigen. *J. W. McLeod*

UHR, J. W. & SCHARFF, M. **Delayed Hypersensitivity. V. The Effect of X-Irradiation on the Development of Delayed Hypersensitivity and Antibody Formation.** *J. Exper. Med.* 1960, July 1, v. 112, No. 1, 65–76, 2 text figs. & 3 figs. on 3 pls. [22 refs.]

"The capacity to develop the delayed type of hypersensitivity to diphtheria toxoid and ovalbumin may persist in guineapigs and rabbits that have received doses of x-ray sufficient to eliminate a detectable antibody response. Larger doses of x-irradiation can prevent development of delayed-type hypersensitivity in rabbits."

ŠLOPEK, S.; SKURSKI, A.; MICHALSKA, E.; DABROWSKI, L.; OBST, B. **Studies on the Mechanisms of the Phagocytic Reaction. I. Phagocytosis and the Antigenic Structure of Gram-Negative Bacilli** [SLOPEK, SKURSKI, MICHALSKA & DABROWSKI]. *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 4, 382–8. **II. Phagocytosis and S-R Dissociation of Gram-Negative Bacilli** [SKURSKI, SLOPEK, MICHALSKA & OBST]. *Ibid.*, 389–92.

I. The authors examined the phagocytosis of several strains of organisms belonging to the Enterobacteriaceae

in order to determine whether the protective effect of surface antigens on the O antigens against agglutination also influenced phagocytosis. The strains studied included Vi-positive and Vi-negative typhoid bacilli; a paratyphoid B culture possessing M antigen; *Shigella* cultures containing surface antigens A or B and also Flexner strains which do not possess the ordinary surface antigens; *Klebsiella* with A antigen and enteropathogenic *coli* possessing B antigens. These various K antigens have different degrees of thermolability, but when fully active they all have some interfering effect on the agglutinability of the living organism carrying them and it was also found that they exert a pronounced inhibitory effect on phagocytosis. Complete inactivation of this inhibitory effect was, however, obtained by heating the bacterial susension in accordance with the thermolability of the particular surface antigen present.

II. It was found that whereas smooth strains of organisms were phagocytosed by horse leucocytes only in the presence of horse serum, the phagocytosis of rough strains occurred without the presence of serum. In the case of *Shigella sonnei* phagocytosis was a sensitive method of determining the degree of dissociation, Phase I–Phase II. *H. J. Bensted*

LINZ, R. & MANDELBAUM, E. Sur la phagocytose *in vitro* des bactéries par les leucocytes de cobaye. II. Avidité des phagocytes pour les bactéries. [*In vitro* **Phagocytosis of Bacteria by Guineapig Leucocytes. II. Avidity of Phagocytes for Bacteria**] *Ann. Inst. Pasteur.* 1960, May, v. 98, No. 5, 664–75.

Continuing their *in vitro* experiments on phagocytosis by guineapig leucocytes in mixtures of *Escherichia coli* and *Staphylococcus albus* [this *Bulletin,* 1960, v. 35, 211], the authors found that certain leucocytes remained "empty", not because they are incapable of phagocytosis, but because of a less pronounced "avidity". Although they do not phagocytose bacteria of one species, leucocytes may possess a greater avidity for bacteria of another species. Although morphologically identical, such leucocytes probably have qualitative differences. As a rule those leucocytes which contain the greatest number of bacteria are the most avid, and easily phagocytose new bacteria of the same species and often bacteria of another species.

Leucocytes capable of phagocytosis may therefore show differences in the specificity and intensity of their avidity for bacteria. *D. A. Cannon*

Notice

Consideration has from time to time been given to the question whether it would be desirable to include authors' addresses in the headings of abstracts in the *Bulletins* and it has been decided that the additional time and cost involved would not be justified. Subscribers are advised, however, that the Bureau will, on request, notify them of the name and address of the author of the article, or the publisher of the journal, from which an abstract has been made.

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